ATP Synthases: Insights Into Their Motor Functions From Sequence and Structural Analyses

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ATP synthases are motor complexes comprised of F_0 and F_1 parts that couple the proton gradient across the membrane to the synthesis of ATP by rotary catalysis. Although a great deal of information has been accumulated regarding the structure and function of ATP synthases, their motor functions are not fully understood. For this reason, we performed the alignments and analyses of the protein sequences comprising the core of the ATP synthase motor complex, and examined carefully the locations of the conserved residues in the subunit structures of ATP synthases. A summary of the findings from this bioinformatic study is as follows. First, we found that four conserved regions in the sequence of γ subunit are clustered into three patches in its structure. The interactions of these conserved patches with the α and β subunits are likely to be critical for energy coupling and catalytic activity of the ATP synthase. Second, we located a four-residue cluster at the N-terminal domain of mitochondrial OSCP or bacterial (or chloroplast) δ subunit which may be critical for the binding of these subunits to F₁. Third, from the localizations of conserved residues in the subunits comprising the rotors of ATP synthases, we suggest that the conserved interaction site at the interface of subunit c and δ (mitochondria) or ε (bacteria and chloroplasts) may be important for connecting the rotor of F₁ to the rotor of F_0 . Finally, we found the sequence of mitochondrial subunit b to be highly conserved, significantly longer than bacterial subunit b, and to contain a shorter dimerization domain than that of the bacterial protein. It is suggested that the different properties of mitochondrial subunit b may be necessary for interaction with other proteins, e.g., the supernumerary subunits.

KEY WORDS: F₀F₁ ATP synthase; biological motor; protein sequence alignment; bioinformatics.

INTRODUCTION

ATP synthases are rotary motor complexes that play a central role in oxidative or photosynthetic phosphorylation, coupling the flow of protons down an electrochemical gradient to the synthesis of ATP. ATP synthases are composed of two discrete sectors (F_1 and F_0) that are considered to be separate rotary motors working cooperatively (for reviews, see Capaldi and Aggeler, 2002; Pedersen *et al.*, 2000a). The essential part of the F_1 motor is an ATPdriven $\alpha_3 \beta_3 \gamma$ subcomplex in which the rotor (γ subunit) is held by a stator $\alpha\beta$ trimer. In the core unit of the F₀ motor that is composed of ac_{10-14} , the proton-driven subunit *c* ring rotor rotates relative to the stator (*a* subunit).

The simplest ATP synthases, i.e. those from nonphotosynthetic eubacterial sources are composed of eight different subunit types (Fillingame and Divall, 1999), which appear to be the minimal composition required for activity. The chloroplast and photosynthetic bacterial ATP synthases consist of nine different subunit types (Borghese *et al.*, 1998; Richter *et al.*, 2000). The mitochondrial ATP synthase is more complicated, as the animal and yeast (or fungal) enzymes are reported so far to consist of 16 and 20 different subunit types, respectively (Pedersen *et al.*, 2000b; Velours and Arselin, 2000). In addition, a potential regulator named STF₃ has been identified recently in yeast from a Blast search of the yeast genome and EST database (Hong and Pedersen, 2002) (Fig. 1).

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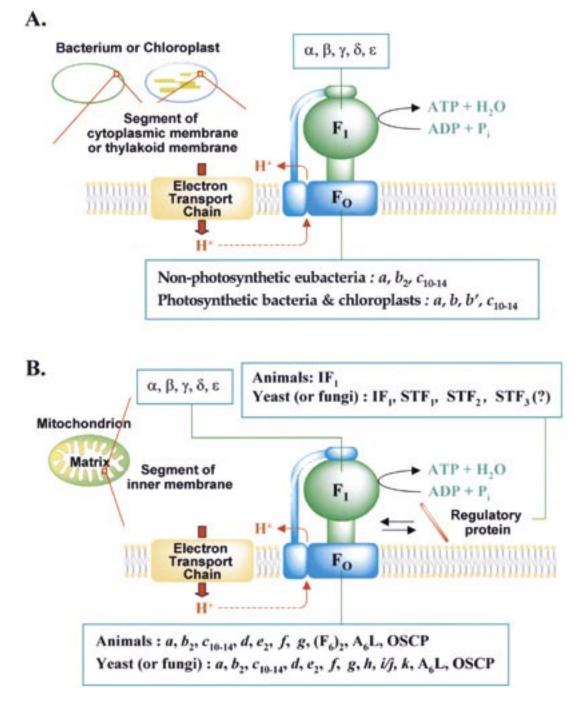


Fig. 1. Schematic structure of F_0F_1 ATP synthase from bacteria and chloroplasts (A) and mitochondria (B).

During the last decade, great strides have been made in understanding the structure of ATP synthases, a result in part from the convergence of biochemical and biophysical studies that have provided valuable information about the structures of these enzymes. Recently, the visualization of the rotation of F_1 using a video microscopic techniqe provided direct evidence for the rotation of the γ subunit within the F_1 motor of an ATP synthase (Noji *et al.*, 1997; Tanabe *et al.*, 2001). Despite this and other remarkable progress, much more work needs to be carried out to fully understand the complicated motor function of ATP synthase. To gain structural insight into the rotary motor functions of ATP synthases, we performed alignments and analyses of the protein sequences that comprise the motor components of ATP synthases. From these studies together with an examination of conserved residues and structural motifs within the available X-ray crystallographic and NMR structures, we found several intriguing structural features that may be related to the motor functions of ATP synthases.

MATERIALS AND METHODS

The protein sequences of the subunits of ATP synthase were retrieved using PSI-BLAST database search (Altschul et al., 1997; Altschul and Konini, 1998) with the default parameters (BLOSUM62 matrix, 0.005 as an E-value threshold, no low complexity filtering in the query sequence) on the nonredundant (nr) protein database. The protein sequences were aligned by the programs ClustalW (Thompson, 1994) and Macaw (Schuler et al., 1991) followed by manual adjustment. The sequence analyses for the prediction of secondary structure, transmembrane helices, and structural motifs were performed using pSAAM (Crofts, 1992), Peptool (Wishart et al., 2000), OMIGA (Kramer, 2001), SOSUI (Hirokawa et al., 1998), TMHMM (Krogh et al., 2001), Coiled-coil prediction server (Lupas et al., 1991), and PredicProtein server (http://www.emblheidelberg.de/ predictprotein/predictprotein.html). The programs WebLab ViewerPro and Ouanta were used for the representation of protein structures. The full names of the species of which the protein sequences are used in this study are [Fungi] A. bisporus-Agaricus bisporus, K. lactis-Kluyveromyces lactis, N. crassa-Neurospora crassa, S. pombe—Schizosaccharomyces pombe, Yeast-Saccharomyces cerevisiae; [Euglenozoa] E. gracilis—Euglena gracilis; [Metazoa] African clawed frog-Xenopus laevis, Bovine-Bos taurus, С. elegans-Caenorhabditis elegans, Fruit fly-Drosophila melanogaster, Human—Homo sapiens, Mouse—Mus musculus, Rat—*Rattus* norvegicus; [Haptophyceae] О. neapolitana—Ochrosphaera neapolitana; [Red Algae] Antithamnion sp., C. caldarium—Cyanidium caldarium, P. purpurea— Porphyra purpurea; [Stramenopiles] O. sinensis— Odontella sinensis, P. littoralis-Pylaiella littoralis, P. tricornutum—Phaeodactvlum tricornutum, [Crvptomonads] G. theta—Guillardia theta; [Green plants] A. columnaris—Aegilops columnaris, Alfalfa—Medicago sativa, A. thaliana-Arabidopsis thaliana, Barley-

Hordeum vulgare, C. reinhardtii—Chlamydomonas reinhardtii, C. vulgaris-Chlorella vulgaris, Japanese black pine-Pinus thunbergii, Liverwort-Marchantia polymorpha, Maize-Zea mays, Norway spruce-Picea abies, Pea-Pisum sativum, Pineapple-Ananas comosus, Rice-Oriza sativa, Sorghum-Sorghum bicolor, Spinach-Spinacia oleracea, Sweet potato-Ipomoea batatas, Tobacco-Nicotiana tabacum, Wheat—Triticum aestivum; [Bacterial] A. aeolicus— Aquifex aeolicus, A. ferrooxidans—Acidithiobacillus ferrooxidans, Anabaena PCC7120, A. tumefaciens-Agrobacterium tumefaciens, Bacillus sp. PS3, B. aphidicola-Buchnera aphidicola, B. caldotenax-Bacillus caldotenax, B. firmus—Bacillus firmus, B. halodurans—Bacillus halodurans, B. megaterium— Bacillus megaterium, B. pseudofirmus-Bacillus pseudofirmus, B. stearothermophilus-Bacillus stearothermophilus, B. subtilis-Bacillus subtilis, Buchnera sp. APS, C. acetobutylicum—Clostridium acetobutylicum, C. jejuni–Campylobacter jejuni, E. coli–Escherichia coli, E. hirae-Enterococcus hirae, H. influenzae-Haemophilus influenzae, H. pylori—Helicobacter pylori, L. acidophilus-Lactobacillus acidophilus, gallisepticum—Mycoplasma gallisepticum, M. М. genitalium—Mycoplasma genitalium, M. leprae— Mycobacterium leprae, M. thermoacetica-Moorella thermoacetica, M. tuberculosis-Mycobacterium tuberculosis, N. meningitidis Z2491-Neisseria meningitidis Z2491, P. aeruginosa—Pseudomonas aeruginosa, P. didemni-Prochloron didemni, P. modestum-Propionicigenium modestum, P. multocida—Pasteurella multocida, R. blasticus-Rhodobacter blasticus, R. capsulatus—Rhodobacter capsulatus, R. prowazekii— Rickettsia prowazekii, R. rubrum—Rhodospirillum rubrum, S. bovis-Streptococcus bovis, S. lividans-Streptomyces lividans, S. mutans—Streptococcus mutans, S. typhimurium—Salmonella typhimurium, Synechococcus PCC6716, Synechocystis PCC6803, T. ferrooxidans-Thiobacillus ferrooxidans, T. maritima—Thermotoga maritima, V. alginolyticus-Vibrio alginolyticus, V. cholerae, X. cholerae—Vibro fastidiosa—Xylella fastidiosa.

RESULTS AND DISCUSSION

Interaction of the γ Subunit With the α and β Subunits

The sequence alignment of the γ subunit shows that the overall sequence is not that conserved in comparision to the α and β subunits although subunit γ is one of the essential subunits for the function of the F_1 motor (Fig. 2). In the sequence alignments of the γ subunits from different sources, the completely and highly conserved residues are distributed fairly clustered, and the clustered regions are primarily localized in the upper and middle regions of the paddle-like structure of this subunit. The lower part of the γ structure as it protrudes from the bottom of F₁ comprises the middle part of the sequence. It contains few completely or highly conserved residues. The residues conserved completely or completely with single variation are found in more than 95% of the 27 protein sequences analyzed. These are clustered into four regions in the sequence of γ (I, 19–26; II, 85–88; III, 238–253; IV, 264–282 in E. coli sequence). It was previously suggested from a suppression mutagenesis study that three segments in the sequence of γ subunit (18–35, 236–246, 269-280 in E. coli sequence) were critically involved in the energy coupling and catalytic activity of ATP synthase (Nakamoto and Al-Shawi, 1995). The three segments suggested in the paper correspond to I, III, IV regions in this study. The region II, which is unique in this study, is also believed to be important for the function of ATP synthases. The four conserved regions of the γ subunit are rearranged into three patches in the structure of γ . Three of the conserved regions, I, II, and III, congregate into a conserved patch (A) in the middle of the γ structure, and region IV segregates into two patches (B and C) at the upper part of γ (Fig. 3(A)).

In α and β subunits, on the other hand, the residues conserved completely or completely with single variation are largely localized on the side facing the γ subunit, covered by nonconserved and weakly conserved residues. Among the conserved α and β residues, those located at the interface with the γ subunit directly interact with the three conserved patches of this subunit (Fig. 3(B)). The conserved regions of α and β subunits from residues S274 to G288, and E253 to L271 in the E. coli sequence, respectively, interact with the conserved patch C of the γ subunit. The conserved residues G335 to F340 of α and Y297 to T310 of β interact with the conserved patch B of the γ subunit. Residues A405 to D414 of α and D372 to K387 of β located in the α -helical domains of these subunits interact with the conserved patch A of γ . Significantly, the three conserved patches of the γ subunit interact differently with the three different conformational forms of the α and β subunits (TP, DP, and E) (Fig. 3(B)). The localized distribution of conserved residues in the γ subunit and the differential patterns of interactions of the three conserved patches of this subunit with the α and β subunits strongly suggest that these specific interactions may be crucial for the rotary motor function of F₁.

The Potential Interaction Site of OSCP (Mitochondria) or δ (Bacteria and Chloroplasts) With F_1

It has been reported that the mutation of the residue Arg94 of rat OSCP caused defects in the interactions of OSCP with F_1 (Golden and Pedersen, 1998). Another study with bovine OSCP showed the same mutational effects when the N-terminal 28 amino acid residues of bovine OSCP were deleted (Joshi *et al.*, 1996). In an attempt to better define the potential interaction sites of OSCP with F_1 , we aligned the sequences of OSCP with those of the δ subunit (OSCP equivalent) from bacteria and chloroplasts, and then examined carefully the conserved residues in the structure of the δ subunit's N-terminal domain (1aby; Wilkens *et al.*, 1997).

In the N-terminal domain structure of the bacterial δ subunit, the region corresponding to the N-terminal 28 residues in OSCP, forms an N-terminal α -helix, and residue 84, which corresponds to the residue 94 in OSCP, is located within a loop connecting two other helices (Fig. 4(A)). In the sequence alignment of OSCP (mitochondria) and the δ subunit (bacteria and chloroplasts), the N-terminal domain structure of the bacterial δ subunit includes four highly conserved residues. Three of these (Tyr10, Ala11, Ala13 in the E. coli sequence) are seen in the N-terminal α -helix (Fig. 5). The other conserved residue in the N-terminal domain structure, Arg84 in the E. coli sequence, is positioned closely to the three conserved residues in the N-terminal α -helix. The detailed examination of the four residues in the N-terminal domain structure lead us to find that the residues Tyr10, Ala13, and Arg84 are aligned in a row on the surface of the structure (Fig. 4(B)). The residue Ala11 is located within the molecule behind the three residues. This four-residue cluster is the only conserved site in the 105 amino acid residue N-terminal domain. Most of the weakly conserved residues within the domain are also positioned around the four-residue conserved cluster. From the arrangement of conserved residues, we suggest that the four-residue conserved cluster plays an essential role in the interaction of OSCP or the bacterial/chloroplast δ subunit with F₁ (Fig. 4(C)).

Specific Interaction Sites at the Interface of the F_1 and F_0 Rotors

In ATP synthases, the rotor of the F_1 motor and the rotor of the F_0 motor are generally considered to be comprised respectively of the $\gamma \varepsilon$ subunit pair (or $\gamma \delta$ in mitochondria) and the *c* subunit ring. The two rotors have been

Yeast	MLSRIVSNNATRSVMCHQAQVGILYKT	NPVRTYA		
"K. lactis	MFVRNTASVVR			
S. pombe	MLROTLTOASRMRPCISVVGFRGFH	ASSPCEA		
Rat		MA		
Bovine	MFSRAGVAGLSAWTVQPQW	IOVRNMA		
Human	MFSRAGVAGLSAWILOPOWIQVRNMAT			
A. thaliana	MIAAIRSPLSSD0EEGLLGVRSIS			
"Sweet potato	MAMAALRREGRRLAAAPFTSPTPLNALRSSLVSPSEEIG			
A. thaliana	MACSNLTTMWVSSKPSLSADSSSLSFRSVLKCPTNTSSPPSRAS			
Tobacco	MSCSNLTMLVSSKPSLSDSSALSFRSSVSPFOLPNHNTSGPSNPSRSS			
Pea	MSCSNVTMLVSSKPSLPDASNLSFRSAFNPFQLPSQNSSSSCTPSRP-			
Spinach	MACSLSFSSSVSTFHLPTTTOSTOAPPNNATTLPT			
C. reinhardtii	MAAMLASKQGAFMGRSSFAPAPKGVASR			
O. sinensis	MALLASKOGAE HORSET AF NOVASK MKFFCVAGLLASAAAFQAQPAAFTTYSPAVGGATSNVFSESSSPAHRNRR			
P. tricornutum	MRSFCIAALLAVASAFTTOPTSFTVKTANVGERASGVFPEQSS-AHRTRK			
	MRECIMULAVADALITOLISTIVATARVOLADOVERLOS	MILLYPIDG		
R. capsulatus	0	ent		
M. genitalium A. acolicus	A	AVI		
		ADI		
H. pylori	8			
C. acetobutylicum	N=====================================	AGA		
Bacillus sp. PS3	N	KPLA		
B. firmus	M	P		
M. thermoacetica	M	P		
V. alginolyticus	М	A		
H. influenzae	М	A		
T. ferrooxidans	N	}		
E. coli		1		
	11 _21_ 31 41 51	1		
"L. coli	11 21 31 41 51 LKEVENRLKSIKNIEKITKIKAST-RLSKAEKAKISAKKMDEAEQLFYK	INAETKNI		
"Yeast				
Yeast K. lactis	LKEVEMRLKSIKNIEKITKTHKIVAST-RLSKAEKAKISAKKMDEAEQLFYK	NAETVPI		
"Yeast "K. lactis "S. pombe "Rat	LKEVENRLKSIKNIEKITKTMKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKTMKIVAST-RLSKAERAKNSAKEYALADAAFYK	NAETVPI EAGTKAI		
"Yeast "K. lactis "S. pombe	LKEVEMRLKSIKNIEKITKIKAIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKIKAIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKIIKTIKTVAQT-KLTRAQRAMEASNKYYRVSDEVFK	NAETVPI EAGTKAI KAEIKGI		
"Yeast "K. lactis "S. pombe "Rat	LKEVEMRLKSIKNIEKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKIKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIKTVAQT-KLTRAQRAMEASNKYYRVSDEVFK LKDITRRLKSIKNIQKITKS <mark>H</mark> KMVAAA-KYARAERELKPARVYGTGSLALYE	NAETVPI EAGTKAI KAEIKGI KADIKTI		
"Yeast "K. lactis "S. pombe "Rat "Bovine	LKEVEMRLKSIKNIEKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKIKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIIKIVAQT-KLTRAQRAMEASNKYYRVSDEVFK LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI		
"Yeast "K. lactis "S. pombe "Rat "Bovine "Human	LKEVEMRLKSIKNIEKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIIKTVAQT-KLTRAQRAMEASNKYYRVSDEVFK LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGUGSLALYE	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI DNPSIDV		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana	LKEVEMRLKSIKNIEKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKIKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIIKIVAQT-KLTRAQRAMEASNKYYRVSDEVFK LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGUGSLALYE TQVVRNRMKSVKNIQKITKAMKYVAAS-KLRAVQGRAENSRGLWQPFTALLG	NAETVPI EAGTKAH KAEIKGH KADIKTH KADIKGH DNPSIDV DTPSVDV		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato	LKEVEMRLKSIKNIEKITKITKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIIKTVAQT-KLTRAQRAMEASNKYYRVSDEVFK LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGUGSLALYE TQVVRNRMKSVKNIQKITKANKYVAAS-KLRAVQGRAENSRGLWQPFTALLG TQVVRNRMKSVKNIQKITKANKYVAAS-KLRAIQTRAENSRGLWQPFTALLG	NAETVPI EAGTKAH KAEIKGI KADIKTI KADIKGI DNPSIDV DTPSVDV NINEQLQ		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana	LKEVEMRLKSIKNIEKITKITKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIIKTVAQT-KLTRAQRAMEASNKYYRVSDEVFK LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE TQVVRNRMKSVKNIQKITKSKKYVAAA-KYARAERELKPARIYGLGSLALYE TQVVRNRMKSVKNIQKITKAKKYVAAS-KLRAVQGRAENSRGLMQPFTALLG TQVVRNRMKSVKNIQKITKAKKYVAAS-KLRAIQTRAENSRGLMQPFTALLG LKDITBRLKSIKNIQKITKAKKYVAAS-KLRAIQTRAENSRGLMQPFTALLG	NAETVPI EAGTKAH KAEIKGH KADIKTH KADIKGH DNPSIDV DTPSVDV NINEQLQ NINEQLQ		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea	LKEVEMRLKSIKNIEKITKITKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIIKTVAQT-KLTRAQRAMEASNKYYRVSDEVFK LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGVGSLALYE TQVVRNRMKSVKNIQKITKSKKYVAAA-KYARAERELKPARIYGLGSLALYE TQVVRNRMKSVKNIQKITKAKKYVAAS-KLRAVQGRAENSRGLMQPFTALLG TQVVRNRMKSVKNIQKITKAKKYVAAS-KLRAVQGRAENSRGLMQPFTALLG LKDIDSVKNTQKITEAMKLVAAS-KLRAVQEAVNGRPFSETLVEVLY LRDRIESVKNTQKITEAMKLVAAS-KVRRAQEAVNGRPFSETLVEVLY	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI DNPSIDV DTPSVDV NINEQLQ SINEQLQ		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco	LKEVEMRLKSIKNIEKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKIKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIKTVAQT-KLTRAQRAMEASNKYYRVSDEVFK LKDITERLKSIKNIQKITKSKKVVAAA-KYARAERELKPARVYGVGSLALYE LKDITERLKSIKNIQKITKSKKVVAAA-KYARAERELKPARVYGVGSLALYE TQVVRNRMKSVKNIQKITKSKVVAAA-KYARAERELKPARVYGVGSLALYE TQVVRNRMKSVKNIQKITKANKVVAAS-KLRAVQGAENSRGLMQPFTALLG TQVVRNRMKSVKNIQKITKANKVVAAS-KLRAVQGAENSRGLMQPFTALLG TQVVRNRMKSVKNIQKITKANKVVAAS-KLRAVQGAENSRGLMQPFTALLG LRELRORIDSVKNTQKITEAMKLVAAA-KVERAQEAVVGREFSETLVEVLY LKDLERIESVKNTQKITEAMKLVAAA-KVERAQEAVVGREFSETLVEVLY LKDLENRIGSVKNTQKITEAMKLVAAA-KVERAQEAVVGREFSETLVEVLY LKDLENRIGSVKNTQKITEAMKLVAAA-KVERAQEAVVGREFSETLVEVLY	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI DNPSIDV DTPSVDV NINEQLQ SINEQLQ NMNEQLQ		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii	LKEVEMRLKSIKNIEKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKIKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIKIVAAT-KLTRAQRAMEASNKYYRVSDEVFK LKDITERLKSIKNIQKITKSKEVVAAT-KYARAERELKPARVYGVGSLALYE LKDITERLKSIKNIQKITKSKEVVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKSKEVVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKAKEVVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKAKEVVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKAKEVVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKAKEVVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKAKEVVAAT-KVERAQEAVVNGREFSELVEVLY LRDLRDRIESVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY LKDLENRIDSVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY LKDLENRIDSVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY LKEVERRIASVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY LKEVERRIASVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI DNPSIDV DTPSVDV NINEQLQ SINEQLQ GVNQRVF		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis	LKEVEMRLKSIKNIEKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKIKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKIKIVAAT-KLTRAQRAMEASNKYYRVSDEVFK LKDITERLKSIKNIQKITKSKEVVAAT-KYARAERELKPARVYGVGSLALYE LKDITERLKSIKNIQKITKSKEVVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKSKEVVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKAKKVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKAKKVAAT-KYARAERELKPARVYGVGSLALYE TQVVENRMKSVKNIQKITKAKKVAAT-KYARAERELKPARIYGLGSLALYE TQVVENRMKSVKNIQKITKAKKVAAT-KYARAERELKPARIYGLGSLALYE TQVVENRMKSVKNIQKITKAKKVAAT-KYARAERELKPARIYGLGSLALYE LKDLENGRISVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY LKDLENGRISVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY LKDLENGRISVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY LKEVEDRIASVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY LKEVEDRIASVKNTQKITEAMKLVAAT-KVERAQEAVVNGREFSELVEVLY ANAIRDRITSVKNTQKITDAMKLVAAT-KVERAQEAVVNGREFSELVEVLY	NAETVPI EAGTKAH KAEIKGH KADIKTH KADIKGH DNPSID DTPSVD NINEQLQ SINEQLQ GVNQRVF GLIARMO		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis P. tricornutum	LKEVEMRLKSIKNIEKITKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIQKITKSKAVAAA-KYARAERELKPARVYGTGSLALYE LKDITERLKSIKNIQKITKSKAVAAA-KYARAERELKPARVYGTGSLALYE LKDITERLKSIKNIQKITKSKAVAAA-KYARAERELKPARVYGTGSLALYE TQVVENRMKSVKHIQKITKSKAVAAA-KYARAERELKPARIYGLGSLALYE TQVVENRMKSVKHIQKITKAKAVAAA-KYARAERELKPARIYGLGSLALYE TQVVENRMKSVKHIQKITKAKAVAAA-KYARAERELKPARIYGLGSLALYE TQVVENRMKSVKHIQKITKAKAVAAA-KYARAERELKPARIYGLGSLALYE TQVVENRMKSVKHIQKITKAKAVAAA-KYARAERELKPARIYGLGSLALYE TQVVENRMKSVKHIQKITKAKAVAAA-KVARAQEAVVNGREFSETLVEVLY LRELERDRIDSVKHTQKITEAMKLVAAA-KVERAQEAVVNGREFSETLVEVLY LKDLKRIDSVKHTQKITEAMKLVAAA-KVERAQEAVVNGREFSETLVEVLY LKELERDRIGSVKHTQKITEAMKLVAAA-KVERAQEAVVNGREFSETLVEVLY LKEVEDRIASVKHTQKITEAMKLVAAA-KVERAQEAVVNGREFSETLVEVLY ANAIRDRITSVKNTKKITMAKLVAAA-KVERAQEAVVNGREFSETLVEVLY	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI DNPSIDV DTPSVDV NINEQLC NINEQLC GVNQRVE GLIARMC GLIQRLC		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis P. tricornutum R. capsulatus	LKEVEMRLKSIKNIEKITKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKITKIVAAT-KUTRAQRAMEASNKYYRVSDEVFK LKDITRRLKSIKNIQKITKSKKWVAAA-KYARAERELKPARVYGVGSLALYE LKDITRRLKSIKNIQKITKSKKWVAAA-KYARAERELKPARVYGVGSLALYE TQVVRNEMKSVKNIQKITKSKKWVAAA-KYARAERELKPARVYGVGSLALYE TQVVRNEMKSVKNIQKITKSKKWVAAA-KYARAERELKPARIYGLGSLALYE TQVVRNEMKSVKNIQKITKAKKWVAAS-KLRAVQGRAENSRGLWQPTTALLG TQVVRNEMKSVKNIQKITKAKKWVAAS-KLRAVQGRAENSRGLWQPTTALLG LRELRDRIDSVKNTQKITEAMKLVAAA-KVRAQEAVVNGREFSETLVEVLY LKDLRDRIESVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKDLKNRISVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY ANAIRDRITSVKNTKKITMAKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKDLKNRIVSVKNTKKITMAKLVAAA-KVRRAQDAVLATREFSETLQSVFG ANAIRDRITSVKNTKKITMAKLVAAA-KVRRAQDAVLATREFSETLQSVFG	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI DNPSIDV DTPSVDV NINEQLC NINEQLC GUNQRVG GLIARMC GLIQRLC SLAGAVC		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis P. tricornatum R. capsulatus M. genitalium	LKEVEMRLKSIKNIEKITKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKITKIVAAT-KYARAERELKPARVYGYGSLALYE LKDITERLKSIKNIQKITKSKKWVAAT-KYARAERELKPARVYGYGSLALYE LKDITERLKSIKNIQKITKSKKWVAAT-KYARAERELKPARVYGYGSLALYE TOVVENEMKSVKHIQKITKSKKWVAAT-KYARAERELKPARVYGYGSLALYE TQVVENEMKSVKHIQKITKSKKWVAAT-KYARAERELKPARVYGUGSLALYE TQVVENEMKSVKHIQKITKAKKWAAT-KYARAERELKPARVYGUGSLALYE TQVVENEMKSVKHIQKITKAKKWAAT-KYARAERELKPARVYGUPTALLG TQVVENEMKSVKHIQKITKAKKWAAT-KVERAQEAVVNGREFSETLVEVLY LRELEDRIDSVKHTQKITEAMKLVAAT-KVERAQEAVVNGREFSETLVEVLY LKDLENRIDSVKHTQKITEAMKLVAAT-KVERAQEAVVNGREFSETLVEVLY LKDLENRIDSVKHTQKITEAMKLVAAT-KVERAQEAVVNGREFSETLVEVLY LKDLENRIGSVKHTQKITEAMKLVAAT-KVERAQEAVVNGREFSETLVEVLY LKDLENRIGSVKHTQKITEAMKLVAAT-KVERAQEAVVNGREFSETLVEVLY ANAIRDRITSVKNTKKITMAKLVAAT-KVERAQEAVVNGREFSETLVEVLY ANAIRDRITSVKNTKKITMAKLVAAT-KVERAQEAVVNGREFSETLVEVLY ANAIRDRITSVKNTKKITMAKLVAAT-KVERAQEAVVNGREFSETLVEVLY LKDLKNRIVSVKNTKKITMAKLVAATSVERAQDAVLATREFSETLOSVG ANAIRDRITSVKNTKKITMAKLVAATSVERAQDAVLATREFSETLOSVG LKDLKNRIVSVKNTRKITKAMAKLVAATSVERAQEAVERAQEAREFSETLVEVLY	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI DNPSIDV DTPSVDV NINEQLC NINEQLC SINEQLC GVNQRVG GLIARMC GLIQRLC SLAGAVC VVVSLKE		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis P. tricornutum R. capsulatus M. genitalium A. aeolicus	LKEVEMRLKSIKNIEKITKIKITKIKA AAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKIKITKAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKITKIAAST-RLSKAERAKNSAKEYALADAAFYK LKDITTRLKSIKNIQKITKSKKVVAAS-KVARAERELKPARVYGVGSLALYE LKDITTRLKSIKNIQKITKSKKVVAAS-KVARAERELKPARVYGVGSLALYE LKDITTRLKSIKNIQKITKSKVVAAS-KVARAERELKPARVYGVGSLALYE TQVVRNMKSVKNIQKITKSKVVAAS-KLRAVQGRAENSRGLMQPFTALLG TQVVRNMKSVKNIQKITKANKVVAAS-KLRAVQGRAENSRGLMQPFTALLG TQVVRNMKSVKNIQKITKANKVVAAS-KLRAVQGRAENSRGLMQPFTALLG TQVVRNMKSVKNIQKITKANKVVAAS-KLRAVQGRAENSRGLMQPFTALLG TQVVRNMKSVKNIQKITKANKVVAAS-KLRAVQGRAENSRGLMQPFTALLG TQVVRNMKSVKNIQKITEANKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LRDLRDRIESVKNTQKITEANKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKDLKNRIDSVKNTQKITEANKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKDLKNRIDSVKNTQKITEANKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITEANKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY ANAIRDRITSVKNTKKITMAMKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITEANKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITTANKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITTANKLVAAA-KVRRAQDAVLATRFFSETLQSVFG ANAIRDRITSVKNTKKITMAMKLVAAA-KVRRAQDAVLATRFFSETLQSVFG ANAIRDRITSVKNTKKITMAMKLVAAA-KVRRAQDAVLATRFFSETLQSVFG LKDLKNRIVSVKNTKKITKANGVVSAA-KLRKAQELVVASRPFSETLVEVLY PRDIKRKIQGIKNTKRITNAMKVVSAA-KLRKAQELVVASRPFSELLSUFVEVLY	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI DNPSIDV DTPSVDV NINEQLC SINEQLC SINEQLC GLIARMC GLIQRLC SLAGAVC VVVSLKE HLAAHVI		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis P. tricornutum R. capsulatus M. genitalium A. aeolicus H. pylori	LKEVEMRLKSIKNIEKITKITKIKIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIQKITKSKAMVAAA-KYARAERELKPARVYGTGSLALYE LKDITFRLKSIKNIQKITKSKAMVAAA-KYARAERELKPARVYGTGSLALYE LKDITFRLKSIKNIQKITKSKAMVAAA-KYARAERELKPARVYGTGSLALYE TQVVRNRMKSVKNIQKITKSKAMVAAA-KYARAERELKPARVYGTGSLALYE TQVVRNRMKSVKNIQKITKSKAMVAAA-KYARAERELKPARVYGTGSLALYE LKDITFRLKSIKNIQKITKSKAMVAAA-KYARAERELKPARVYGTGSLALYE TQVVRNRMKSVKNIQKITKAMKAVAAS-KLRAIQTRAENSRGLMQPFTALLG TQVVRNRMKSVKNIQKITKAMKAVAAS-KLRAIQTRAENSRGLMQPFTALLG TQVVRNRMKSVKNIQKITKAMKAVAAS-KLRAIQTRAENSRGLMQPFTALLG TQVVRNRMKSVKNIQKITKAMKAVAAS-KLRAIQTRAENSRGLMQPFTALLG LRELRDRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY ANAIRDRITSVKNTCKITMAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRISVKNTQKITTAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY ANAIRDRITSVKNTCKITMAMKLVAAA-KVRRAQDAVLATRPFSETLOSVFG LKDLKNRIVSVKNTRKITMAMKLVAAA-KVRRAQDAVLATRPFSETLOSVFG LKDLKNRIVSVKNTRKITMAMKLVAAA-KVRRAQDAVLATRPFSETLOSVFG LKDLKNRIVSTIKITKAMKVYSAA-KVRRAQDAVLATRPFSETLOSVFG LKDLKNRIVSTKNTRKITMAMKLVAAA-KVRRAQDAVLATRPFSETLOSVFG LKDLKNRIVSTKNTRKITMAMKLVAAA-KVRRAQDAVLATRPFSETLOSVFG LKDLKNRIVSTKNTRKITMAMKLVAAA-KVRRAQDAVLATRPFSETLOSVFG LKDLKNRIVSTKNTKKITMAKLVVSAA-KURACELVYASRPYSELLYELVG LRDIRKKIGSVKNTQKITHAMKUVSAA-KLRAQELVYASRPYSELLYELVG LRDIRKKIGSVKNTQKITHAMKUVSAA-KLRAQELVYASRPYSELVELVG	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKTI DNPSID DTPSUD DTPSUD NINEQLO SINEQLO SINEQLO GVNQRVE GLIARMO GLIQRLO SLAGAVO VVVSLKE HLAAHVU DVLSKME		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis P. tricornutum R. capsulatus M. genitalium A. aeolicus H. pylori C. acetobutylicum	LKEVEMRLKSIKNIEKITKITKIKIVASI-RLSKAEKAKISAKHDEAEQLFYK LREIETRLKSIKNIEKITKITKIVASI-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKIVASI-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIQKITKSKYVAAA-KYARAERELKPARVYGTGSLALYE LKDITFRLKSIKNIQKITKSKYVAAA-KYARAERELKPARVYGTGSLALYE LKDITFRLKSIKNIQKITKSKYVAAA-KYARAERELKPARVYGTGSLALYE TQVVRNRMKSVKNIQKITKSKYVAAA-KYARAERELKPARVYGTGSLALYE TQVVRNRMKSVKNIQKITKSKYVAAA-KYARAERELKPARVYGTGSLALYE TQVVRNRMKSVKNIQKITKANGAVAAS-KLRAVQGAENSRGLMQPTALLG TQVVRNRMKSVKNIQKITKANGAVAAS-KLRAVQGAENSRGLMQPTALLG TQVVRNRMKSVKNIQKITKANGAVAAS-KLRAVQGAENSRGLMQPTALLG LRELRDRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITAAKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKEVRDRIASVKNTQKITAAKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKDLKNRIVSVKNTKKITMAKLVAAA-KVRRAQEAVVGRPFSETLVEVLY LKDLKNRIVSVKNTKKITMAKLVAAA-KVRRAQEAVVGRPFSELVEVLY LKDLKNRIVSVKNTKKITMAKLVAAA-KVRRAQEAVVGRPFSELVEVLY LKDLKNRIVSVKNTKKITMAKLVAAA-KVRRAQEAVVGRPFSELVEVLY LKDLKNRIVSVKNTKKITMAKLVAAA-KVRRAQEAVVGRPFSELVEVLY LKDLKNRIVSVKNTKKITMAKLVAAA-KVRRAQEAVVGRPFSELVEVLY LKDLKNRIVSVKNTKKITMAKLVAAA-KVRAQEAVVAARPYAERYAAKA LQIKKIGSVKNTQKITNAMKVSRAKFIKFKAQELVYASRPYSEKLVELVG LRDIKKIGSVKNTQKITHAKKIVSS-KLRKAEVARNSRAYALKLDAVFD LIIIKFRIKSITNTKKITNAMGLIATS-NLRKSRQNLEANKAYYEAFNDVIN	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKTI DNPSIDV DTPSVDV NINEQLC SINEQLC SINEQLC GVNQRVF GLIARMC GLIQLG SLAGAVC VVVSLKE HLAAHVU DVLSKMK KIVSSSS		
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Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis P. tricornutum R. capsulatus M. genitalium A. aeolicus H. pylori C. acetobutyficum Bacillus sp. PS3 B. firmus M. thermoacetica V. alginolyticus	LKEVEMRLKSIKNIEKITKIKIVAAT-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKIKIVAAT-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKIVAAT-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIQKITKSKKWAAA-KYARAERELKPARVYGTGSLALYE LKDITHRLKSIKNIQKITKSKKWAAA-KYARAERELKPARVYGTGSLALYE LKDITHRLKSIKNIQKITKSKKWAAA-KYARAERELKPARVYGTGSLALYE TQVVRNRMKSVKNIQKITKAKKWAAA-KYARAERELKPARVYGTGSLALYE TQVVRNRMKSVKNIQKITKAKKWAAA-KYARAERELKPARVYGTGSLALYE TQVVRNRMKSVKNIQKITKAKKWAAA-KYARAERELKPARVYGDFTALLG TQVVRNRMKSVKNIQKITKAKKWAAA-KYARAERELKPARVYGDFTALLG LRELRDRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKDLRNEDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKDLRNIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKDLRNIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITAMKLVAAA-KVRRAQEAVVNGREFSETLVEVLY LKEVRDRIASVKNTQKITAAKVVSAA-KVRRAQDAVLATREFSETLQSVFG LKDLNNRIVSTIKITNAKVVSAA-KURRAQDAVLATREFSETLQSVFG LKDLNNRIVSTIKITNAKVVSAA-KURAQELVASREFSELVEVUG LKDIRKIGSVKNTQKITHAKVVSAA-KURAQELVASREFSELVEVUG LKDIRKIGSVKNTQKITHAKVINTAKVSAA-KURAASINSRAYALKLDAVFD LIIIKRINATKKTSQITKAMMVISA-KURRAQELVASREFSELVEVVA NRDLKRKISITNIKKITNAKVVSAA-KURRAQAQVTAGREFYAENDVIN LRDIGRITSTKKTKQITKAMMVISA-KURRAQAQVTAGREFYAENDVIN LRDIGRITSTKKTKUTKAMAYAAA-KURRAQAQVTAGREFYAEHVKIG AKEIRNKIGSVKSTQKITKAMAYAAA-KURAAS-KMRRSQDAMEASREFYAEHVKIG AKEIRNKIGSVKSTQKITKAMAYAAA-KURAAS-KMRRSQDAMEASREFYAEHVKIG	NAETVPI EAGTKAI KAEIKGI KADIKTI KADIKGI DNPSIDV DTPSVDV NINEQLQ SINEQLQ SINEQLQ SUQRVF GLIARMO GLIQRLO SLAGAVO VVVSLKE HLAAHVI DVLSKME KIVSSSS NVALA-A AIASSGT RLMAAVI		
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Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis P. tricornutum R. capsulatus M. genitalium A. aeolicus H. pytori C. acetobutylicum Bacillus sp. PS3 B. firmus M. thermoacetica V. alginolyticus H. influenzae T. ferrooxidans	LKEVEMRLKSIKNIEKITKIKITKIKA AST-RLSKAEKAKISAKHDEAEQLFYK LREIETRLKSIKNIEKITKITKIKATAAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKITKIAAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIQKITKSKAMAAA-KYARAERELKPARYYGYGSLALYE LKDITTRLKSIKNIQKITKSKAMAAA-KYARAERELKPARYYGYGSLALYE LKDITTRLKSIKNIQKITKSKAMAAA-KYARAERELKPARYYGYGSLALYE TQVVRNEMKSVKNIQKITKSKAMAAA-KYARAERELKPARYYGYGSLALYE TQVVRNEMKSVKNIQKITKAMKAVAAS-KLRAVQGRAENSRGLMQPTALLG TQVVRNEMKSVKNIQKITKAMKAVAAS-KLRAVQGRAENSRGLMQPTALLG TQVVRNEMKSVKNIQKITKAMKAVAAS-KLRAVQGRAENSRGLMQPTALLG TQVVRNEMKSVKNIQKITKAMKAVAAS-KLRAVQGRAENSRGLMQPTALLG TQVVRNEMKSVKNIQKITKAMKAVAAS-KLRAVQGRAENSRGLMQPTALLG TQVVRNEMKSVKNIQKITKAMKAVAAS-KLRAVQGRAENSRGLMQPTALLG TQVVRNEMKSVKNIQKITKAMKAVAAS-KLRAVQGRAENSRGLMQPTALLG LRELRDRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKDLKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITAAMKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITAAKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITAAKLVAAA-KVRRAQEAVVNGRPFSETLVEVLY LKEVRDRIASVKNTQKITAAKLVAAA-KVRRAQDAVLATRFFSETLQSVFG ANAIRDRITSVKNTKKITMAKLVAAA-KVRRAQDAVLATRFFSETLQSVFG LKDLKNRIVSVKNTKKITMAKLVAAA-KVRRAQEAVVAGRPFSELVEVUG PRDIKRKIGSVKNTQKITHAKIVSSA-KLRKAQELVASRPYSEKLYEUG LKDLKNRIVSVKNTKKITMAKKVVSAA-KLRKAQELVASRPYSEKLYEUG LKDIKRKIGSVKNTQKITHAKIVSS-KLRKAQELVASRPYSEKLYEUG LKDIKRKIGSVKNTQKITHAKIVSSA-KLRKAQELVASRPYSEKLYEUG LKDIKRKIGSVKNTQKITHAKIVSSA-KLNRAQHNAGSFTPYTKIRGEVVA MRDLKRRIRSVQSTQHITRADGVAAA-KLRKAQQVTAGRPYAAKLEEVVG AKEIRKIGSVKSTQKITKAMEMAAS-KMRRSQDAMEASRPYSETIRVIG AKEIRKIGSVKSTQKITKAMEMAAS-KMRRSQDAMEASRPYSETIRVIG AKEIRKIGSVKNTQKITKAKAMAS-KMRRAQERMAARSRPYSETIRVIG AKEIRKIGSVKNTCKITKAMEMAAS-KMRRAQERMAARPCAEKIREVG AKEIRKIGSVKNTCKITKAMEMAAS-KMRRAQERMAARPCAEKIREVG	NAETVPI EAGTKAE KAEIKGE KADIKTE KADIKGE DNPSIDV DTPSUDV DTPSUDV NINEQLQ SINEQLQ GVNQRVE GLINEQLQ GVNQRVE GLINEQLQ GVNQRVE GLINEG SLAGAVG VVVSLKAE HLAAHVD DVLSKMK KIVSSSS NVALA-A AIASSGT RLMAAVD HVANANL HVANANL		
Yeast K. lactis S. pombe Rat Bovine Human A. thaliana Sweet potato A. thaliana Tobacco Pea Spinach C. reinhardtii O. sinensis P. tricornutum R. capsulatus M. genitalium A. aeolicus H. pytori C. acetobutyficum Bacillus sp. PS3 B. firmus M. thermoacetica V. alginolyticus H. influenzae	LKEVEMRLKSIKNIEKITKIKITKASIVAST-RLSKAEKAKISAKKMDEAEQLFYK LREIETRLKSIKNIEKITKITKIKASIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIEKITKITKITKIVAST-RLSKAERAKNSAKEYALADAAFYK LKEIEQRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGTGSLALYE LKDITFRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGTGSLALYE LKDITFRLKSIKNIQKITKSKKYVAAA-KYARAERELKPARVYGTGSLALYE TQVVRNEMKSVKNIQKITKSKKYVAAA-KYARAERELKPARVYGTGSLALYE TQVVRNEMKSVKNIQKITKAKKYVAAA-KYARAERELKPARIYGLGSLALYE TQVVRNEMKSVKNIQKITKAKKYVAAA-KYARAERELKPARIYGLGSLALYE TQVVRNEMKSVKNIQKITKAKKYVAAA-KYARAERELKPARIYGLGSLALYE TQVVRNEMKSVKNIQKITKAKKYVAAA-KYARAQEAVVGREPSETLVEVLY LRELRDRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKELKNRIDSVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKELRDRIGSVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKEVRDRIASVKNTQKITEAMKLVAAA-KVRRAQEAVVGREPSETLVEVLY ANAIRDRITSVKNTRKITMAKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKDIKNRIVSVKNTRKITMAKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKDIKNRIVSVKNTRKITMAKLVAAA-KVRRAQEAVVGREPSETLVEVLY LKDIKRIQGIKNTKKITNAKUVSAA-KLRKAQELVASRPYSELVEUVG LKDIKRKIGSVKNTQKITHAKIVSAA-KLRKAQELVASRPYSELVEUVG LKDIKRKIGSVKNTQKITHAKIVSAA-KLRKAZEVARNSRAYALKLDAVFD LIIIKRRIKSITNTKKITNAKUVSAA-KLRKAZEVARNSRAYALKLDAVFD LIIKRRISVSTQTITAAKVVAAA-KLRKAZEVARNSRAYALKLDAVFI LKDIKRKISVSTQTITAAKVVAAA-KLRKAZEVARNSRAYALKLEVVG AKEIRNKIGSVKSTQKITKAKEMVAAS-KMRRSQDAMEASRPYSETIRVIS AKEIRNKIGSVKSTQKITKAKEMVAAS-KMRASENAASFENGENGASRPYSETIRVIS	NAETVPI EAGTKAP KADIKTP KADIKTP KADIKGP DNPSIDV DTPSUDV DTPSUDV DIPSUDV SINEQLQ SINEQLQ GVNQRVR GLIARMG GLIQRLG SLAGAVG VVVSLKE HLAAHVD DVLSKMK KIVSSSS NVALA-A AIASSGT RLMAAVD HVANANL HVANANL		

Fig. 2. Sequence alignment of the γ subunit. The conserved residues are in bold, and the residues conserved completely, and completely with only a single deviation, are highlighted in shade. Note that the residues conserved completely or completely with a single variation are clustered in four regions in the sequence of γ (I, II, III, and IV). The letters M, C, and B in superscript denote the source of the sequence; mitochondria, chloroplast, and bacteria, respectively.

	71 81 91 101
"Yeast	VEATETGAPKELIVAITSDKGLCGSIHSQLAKAVRHLNDC
"K. lactis	DAEKKDLIIAITSDKGLCGSIHSQLAKAVRLQLKQT
"S. pombe	EGKTLMVACSSDKGLCGGIHSSISRLIRRELHDP-KTF
"Rat	DKKKHLIIGVSSDRCLCCAIHSSVAKOMKNDMAALTAAG
"Bovine	DKKKHLIIGVSSDRGLCGAIHSSVAKOMKSEAANLAAAG
^M Human	DKKKHLLIGVSSDRGLCGAIHSSIAKOMKSEVATLTAAG
^M A. thaliana	KSVVVTL&SDKCLCCGINSTVVKVSRALYKLNAGPE
"Sweet potato	KNVIITISSDKGLCGGINSTSVKTSRNIHKLNSGPE
A. thaliana	DDVDVPLTKVRPVKKVALVVVTGDRGLCGGFNNFIIKKAEARIKELKGLG
Tobacco	DDIDVPLTKVRPVKKVALVVVTGDRGLCGGFNNYLIKKAEARIRDLKALG
Pea	DDIESPLTKLRPVKKVALVVCTGDRGLCGGFNNAILKKAEARIAELKELG
*Spinach	EDVDVPLTKIRTVKKVALMVVTGDRGLCGGFNNMLLKKAESRIAELKKLG
C. reinhardtii	EDVDSPLCAVRFVKSVLLVVLTGDRGLCGGYNNFIIKKTEARYRELTAMG
O. sinensis	EALDLPLLTQREVSKVTLVVITGDRGLCCGYNSFMIKKAEARFNELKDQG
P. tricornutum	ESVDLPLLTEREVKKVTLLVITGDRGLCGGYNSFMIKKAEARFNELKKNG
R. capsulatus	TDGAPRLLAGTGSDKVHLLVINTGERGLCGGFNANIAKLAKAKAMELLAQG
M. genitalium	KKKPDNQKTLWIMMSSSLGLCGQHNSNMNKLLKANFKADDK
A. aeolicus	EDNPLFDVREERNVDVILVTADRGLAGAFNSNVIRTAENLIREKEEKG
H. pylori	QGIEDIQSKYFRELERLEIKKVDIIFITADKGLCGGFNTNTIKKVLACTNEYKEKD
C. acetobutylicum Bacillus sp. PS3	SNLYVAGNKSDKKLYIALTSDSGLCGGFNGAVVTAADNVMRGDKDK- ASHPMLVSRPVKKTGYLVITSDRCLAGAYNSNVLRLVYOTIOKRHASF
B. firmus	ISHPMLEERPVKKTGYLVTSDKGLAGGYNSSLIRSLLNTIKERHNSF
M. thermoacetica	ETOPLAATREVKKAGYVLITADRGLACGYNANLIRLTEERLREEGR
V. alginolyticus	YRHPYLEEREAKRVGYIIVSTDRGLCGGLNINVFKKAVTDMOTWREKG
"H. influenzae	YKHPFLVEREVKKIGILVISTDRGVCGGLNVNLFKTTLNOIKNWKEON
T. ferrooxidans	YEHPLMOVRPVKKAGFLVVTTDRGLCGGLNVNVLRNVVOKMRELHEEG
E. coli	YKHPYLEDRDVKRVGYLVVSTDRGLCGGLNINLFKKLLAEMKTWTDKG
1. CON	71 81 91 101
"Yeast	111 121 131 141 151 16 NADIVTIGDKIKMOLLRTHPNNIKLSINGIGKDAPTFOESALIADKLLSVMKAGTYPKI
"K. lactis	NADVVAIGDKVKGQLLRTNSDNLKFAFNGVGKEAPTFEETSLIANKILEGGAS-NYKKV
"S. pombe	NTSLCILGERVRTOLLRFCPESFYLTFAHIGGASPSFEEALOISSNILEHAKDYDRI
"Rat	EVMIVGIGERIKSILYRTHSDOFLVSFKDVGRKPPTFGDASVIALELLNSGYEFDEG
"Bovine	EVKIIGVGDKIRSILHRTHSDOFLVTFKEVGRRPPTFGDASVIALELLNSGYEFDEG
*Human	EVMLVGIGDKIRGILYRTHSDQFLVAFKEVGRKPPTFGDASVIALELLNSGYEFDEG
"A. thaliana	EVQFVIVGEKAKAIMFRDSKNDIVLSVTELNKNPLNYAQVSVLADDILKNVEFDAL
"Sweet potato	ENKYVILGEKAKAQLVRDSKKDIELIITELQKNPLNYTQVSVVADDILKNVEFDAL
A. thaliana	EYTVISVGKKGNSYFLRR-PYIPVDKYLEAG-TLPTAKEAQAVADDVFSLFISEEVDKV
Tobacco	DYTIISVCKKGNSYFIRR-PYIPVDKFLEGS-NLPTAKDAQAIADDVFSLFVSEEVDKV
Pea	EYTVVSVGRKGNSYFNRR-PYIPVDRFLEGG-SLPTAKEAQTIADDVFSLFVSEEVDKV
Spinach	DYTIISICKKGNTYFIRR-PEIPVDRYFDGT-NLPTAKEAQAIADDVFSLFVSEEVDKV
C. reinhardtii	KVNLVCVGRKGAQYFARR-KQYNIVKSFSLG-AAPSTKEAQGIADEIFASFIAQESDKV
O. sinensis P. tricornutum	ACDMVLICKKGITYFQRR-G-YPIRKTFETG-QNPDSKQALAISEELLNTYLSGESDAV
R. capsulatus	EADLILVORKGIAYFERR-G-FPIRKKYETG-QNPTAKQALAIAEEVSSTFLSGESDAV
^a M. genitalium	TVKILTVCKKCRDALRRDLGQYYIDHIDLSDVKKLSYPVAQKISQNIIDRFEAGEYDVA
A. acolicus	IFFLCRKNQSFWNKNSQYNPAVGFIDIQDRDINFDYCQTIFDQIMDAFKEFKLDRI KVSLILVCRKGFQYFTKR-GYNVIKGYDEVFRKTVNFNVAKEVAEIVKERFLNGETDRV
"H. pylori	KVRLRGIGKKGNEYFSFN-GIEVLDKINNLS-SMPNYERVOEFMKKVVEDYLSGKTDKV
C. acetobutylicum	-SLLITVOCKGISYFKRL-KYETLSEYVDIP-NEPGLKEAKEIADRALSLYEKGEIGEV
Bacillus sp. PS3	EYAIIVIGRVGLSFFRKR-NMPVILDITRLP-DOPSFADIKEIARKTVGLFADGTFDEL
B. firmus	EYGIIIMGRIGRDLFKKR-GLPIIQEVIGLP-DQPEFNDIKNIARTSVEMFADGIFDEL
M. thermoacetica	PAALVAVGRKGRDFFRR-PVEIVKSFTDIG-DNPELIQARELARQLVTNYLEGTLDEV
V. alginolyticus	
	EIELAVVGSKATAFFKHG-GAKVAAQVSGLG-DNPSLEDLIGSVGVMLKKYDEGELDRL
V. alginolyticus H. influenzae T. ferrooxidans	
"H. influenzae	EIELAVVGSKATAFFKHG-GAKVAAQVSGLG-DNPSLEDLIGSVGVMLKKYDEGELDRL STDLGLIGSKGISFFRSF-GFNIKGQLSGLG-DTPALEELIGVANTMFDAYRNGEIDAV
^a H. influenzae ^a T. ferrooxidans	EIELAVVCSKATAFFKHG-GAKVAAQVSGLG-DNPSLEDLIGSVGVMLKKYDEGELDRL STDLGLIGSKGISFFRSF-GFNIKGQLSGLG-DTPALEELIGVANTMFDAYRNGEIDAV ESNLAVVCNKGLGFLRRH-GAHLVADVNGLG-DSPHLGDMIGPIRAMADAYAKGEVDVV

Fig. 2. Continued

171 181 191 ------"Yeast IFYNDPVSSLSFEPSEKPIFNAKTIEOS--K. lactis IFWNDPISSLSFEPSNKPVFNAAAIEOS-----LVYNKFASAVSFETVMKNLYTTKAINES-----S. pombe Rat IIFNQFKSVISYKTEEKPIFSFSTVVAA-----IIFNRFRSVISYKTEEKPIFSLDTISSA-----Bovine Human IIPNKFRSVISYKTEEKPIFSLNTVASA-A. thaliana IVYNKFHSVVAFLPTVSTVLSPEIIEKES-----EI Sweet potato IVFNKFQSVVSFVPTMSTVLSPEVVERES--------- ES A. thaliana LLYTKFVSLVKSEPVIHTLLPLSPKGEICDINGTCVDAAEDEFFRLTTKEGKLTVERETF Tobacco LLYTKFVSLVKSEPVIHTLLPLSPKGEICDINGNCVDAANDEFFRLTTKEGKLTVERDII Pea LLYTKFV\$LVKSNPIIHTLLPLSPKGEICDINGNCVDAAEDELFRLTTKEGKLTVERDVI Spinach MLYTKFVSLVKSDPVIHTLLPLSPKGEICDINGKCVDAAEDELFRLTTKEGKLTVERDNI C. reinhardtii LVFTKFISLINSNPTIQTLLPMTPMGELCDVDGKCVDAADDEIFKLTTKGGEFAVEREKT LLYTKFISLIASSPSARTLIPFS-----ASEITQQGDEVFQLTSSGGDFEVERTEL ^cO, sinensis P. tricornutum LLYTKFVSLIASSPSIRTLVPFS-----ASDITAKGDEVFQLTSESGQFGVERTEL R. capsulatus IFFSVFQSVISQVPTAKQVIPAQ-----MVYTKFKNSLIQQSQLFQVFPFDVETFKT-----⁸M. genitalium LINNEMVTRASYKPQVRVFLPF-----A. aeolicus ---E IIHNGFKNMITQEIRVKTILPIGYK-----IIHON II. pylori VIYTQFLSTVNQKVEVKKVLPIE-----C. acetobutylicum MYYNHYVSAIQQEVTERKLLPLT-----DLA Bacillus sp. PS3 VWYNHFVSPITQDVTEMKLLLLT-----DIG B. firmus [®]M. thermoacetica LINTRFYSPIROVPMVERLLPIA-----TPR VVFNKFVNTMVQQPTIDQLLPLP-----KSD V. alginolyticus IAYNKFVNTMSQKPVVQQLVPLPE-----SKD H. influenzae LVSSRFVNTMLQRATVEQLLPVE-----KPT T. ferrooxidans IVSNKFINTMSQVPTISQLLPLP----ASD E. coli 171 181 191 201 211 221 231 241 "Yeast -----PSFGKFEIDTDANVPRDLFEYTLANOMLTAMAOGYAAEISARRNAMDNASKN K. lactis -----PSFSKFEIDADNNVSQOLFEFTLSNEILAAMAEGYAA VSAL RNA DNASK "S. pombe -----PNLSAYEVS--DEVHOPLMEFAFANAIFSAMAEAHCSE RNAMENASK MSS Rat -----ENMS-IYDDIDADVLQNYQEYNLANIIYYSLKESTTS 03A MTAMDNASK Bovine -----ESMS-IYDDIDADVLRNYQEYSLANIIYYSLKESTTS QSARMTAMDNASKN/ Human ----DSMS-IYDDIDADVLONYQEYNLANIIYYSLKESTTSCOSARMTAMDNASKN/ A. thaliana GGKLGELDSYEIEGGETKGEILONLAEFQFSCVMFNAVLENACSEMGARMSAMDSSSR "Sweet potato GGKLGDLDSYEIEGAESKSEVLQNLTEFQFSSVLFNAVLENACSEQGARMSAMDSSSR A. thaliana RTPTADFSP-ILQFEQDPVQILDALLPLYLNSQILRALQESLAS LAARMSAMSSASD **Tobacco** RTKTTDFSP-ILQFEQDPVQILDALLPLYLNSQILRALQESLAS AARMSAMSSATD Pea RSKTVDFSP-ILQFEQDPVQILDALLPLYLNSQILRPLQESLASE LAAR MSAMSSAFI Spinach KTETPAFSP-ILEFEQDPAQILDALLPLYLNSQILRALQESLASELAAR MTAMSNATE C. reinhardtii TIETEALDP-SLIFEQEPAQILDALLPLYMSSCLLRSLQEALASELAARMNAM WNASI O, sinensis EVAEPODFFNDMIFEODPIOIINSILPLYLNGOILRTLOESVASELAARMOSMOSASI P. tricornutum DVAAPQEFPNDMIFEQDPIQIVNAILPLYLNGQILRTLQESVASELAARMOSMOSASI R. capsulatus FETDAASASAVYDYEPGDQEILTALLPRAVATAIFAALLENNASFNGAQMSAMDNAT M. genitalium --LNPVVTDQQLDFEPDQATIINLITPQFFDVALYGGLVETKLCESASRONAMEAATK A. acolicus AQEKEVEELGTYEFEVSEEEFFDYIVNLYLNYQVYRAMVESNAA HFA MIAMONATH H. pylori POPSETQETITSEPSGSEDEILDSLAEKYVEYSLYYALIDSLAATHSARMOANDTATN C. acetobutylicum -- PKKMEKVSVAEFEPDAEIILEKAIRLHIEQQLFNLLLNSKAS OAS MSS DSATK Bacillus sp. PS3 ENKORT----VYEFEPSQEEILDVLLPQYAESLIYGALLDAKASEHAAFMTAMKNATD B. firmus SDEKATSASASYEYEPNEQAILEKLLPQYAENLIYGSLLDAKASEFGARMTAMSAATD [®]M. thermoacetica EKKDTG----DYIYEPSPEGVLRVLLPRYCEIKVYRALLEAKASEHGARMTAMDNATK V. alginolyticus SEEMOREHSWDYIYE PEPKPLLDTLLVRYVESQVYQGVVENLACEQAARMIAMKAATD H. influenzae DHLNERQQTWDYLYEPEPKVLLDSLLVRYLESQIYQAVVDNVASEQAARMVAMKAATI T. ferrooxidans ASAEQRAELWDY IYE PEAR PVLDRLMORYVESVVYOAVIEHLACE OSAFWVAM KSASI E. coli -DDDLKHKSWDYLYEPDPKALLDTLLRRYVESQVYQGVVENLASEQAARMVAMKAATI 201 211 221 231 ш

Fig. 2. Continued

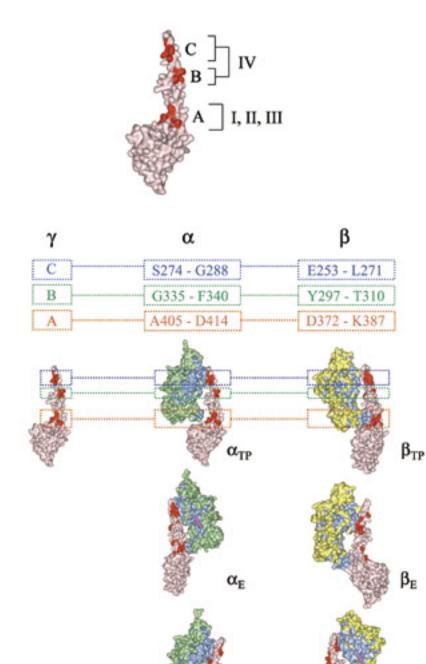
	251	261	271
"Yeast	GDMINRYSILYNE	TROAVITN	ELVDI ITGASSLG
K. lactis	GDMINSYSILYNE	TROAVITN	ELVDIITGASSLD
S. pombe	GDMINKFSIONNE	OROASITN	ELIDIVIGANSLA
Rat	SDMIDKLTLT	TROAVITK	ELIEIISGAAALD
Bovine	SEMIDELTLT	TROAVITK	ELIEIISGAAALD
Human	SEMIDKLTLT	TROAVITK	ELIEIISGAAALD
A. thaliana	GEMLDRLTLTYNE	TROASIT	ELIEIISGASALEAAK
Sweet potato	GENLORLTLTYNE	TROASITT	ELIEIISGASALEG
A. thaliana	SDLKKSLSMVYNR	KROAKITG	EILEIVAGANAQV
Tobacco	TELKKNLSRVYNE	CROAKITG	EILEIVAGADALV
Pea	SELETDLTRVYNE	ATCAKITG	EILEIVAGDIECIIW
Spinach	NELEKTLSINYNE	AROAKITG	EILEIVAGANACV
C. reinhardtii	KELKKGLTVQ YNK	OROAKITO	ELAETVGCAAATSG
O. sinensis	GDLAKRLSTEYNE	ARGAAVIC	EILEIVSGASALE
P. tricornutum	GSLAKQLNLEYNE	AROAAVTO	ELLEIISGASALD
R. capsulatus	GDMIDRLTIEYNE	SROAAITK	ELIEIISGAEAL
M. genitalium	KDLLDKYTLOFNK	LRONSITE	EIIEVIGEMN
A. aeolicus	EDLIRQWTLVFNK	ARCEATT	ELIDITNAVEALKAQ
H. pylori	KDLVKTLTISYNK	ARCEATT	ELVEINAGVEALK
C. acetobutylicum	NDLLDALNIKYNE	IROSAITO	EITEIVGGAEALK
Bacillus sp. PS3	NELIRTLTLSYNE	ARCAAITO	EITEIVAGANALQ
B. firmus	SALIEELTLEFNE	ARCAAITO	EITEIVGCAAALE
M. thermoacetica	AENIDKETLSENE	ARCAALTN	EIVEIVAGADALK
V. alginolyticus	TNLIDDLELVYNK	AROAAITO	ELSEIVGGAAAV
H. influenzae	GNLINDLRLVYNN	AROASITN	ELNEIVAGAAAI
T. ferrooxidans	KRNVDDLQLAYNE	ARGAAITO	EIAEISAGAARFDDCAQHFWRI
E. coli	GSLIKELQLVYNE	AROASITO	ELTEIVSCANAV
Kie CMM	261	271	281

Fig. 2. Continued

reported to behave as one mechanical unit in ATP synthase (Tanabe et al., 2001). In mitochondrial ATP synthase, the ε subunit, the counterpart of which is not present in bacterial or chloroplast ATP synthase, may also be a part of the F₁ rotor. Experimentally, the two motors of ATP synthase, F₁ and F₀ can be easily separated, and also can be reconstituted to form a functional F_0F_1 motor complex. The reversibility of the strip of F_1 , and reconstitution of F_1 and F_0 , indicate that the F_1 rotor and the F_0 rotor have specific sites for interaction. On the basis of the current available X-ray crystal structural data of ATP synthase, one of the potential specific interaction sites is believed to be located at the interfaces between the rotors of F₁ and F_0 where the $\gamma \varepsilon$ (bacteria and chloroplasts) or $\gamma \delta$ (mitochondria) subunits of F₁ rotor have direct contacts with the subunit c ring comprising the F_0 rotor. To gain insight into the potential specific interaction site at the interface

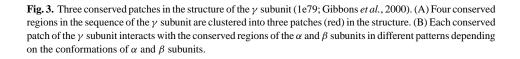
of the rotors of F_1 and F_0 , we aligned the sequences of the three subunit types, γ , δ (mitochondria) or ε (bacteria and chloroplasts), and *c* subunits, and examined the conserved residues at the interfaces of the subunits in the available crystal structures.

The sequence alignment of subunit *c* shows that seven residues are completely or highly conserved, and three of them (Arg41, Gln42 or Asn, and Pro43 in *E. coli* sequence) are located facing F₁ at the interhelical loop (Fig. 6 and 8(A)). In the δ (mitochondria) or ε (bacteria and chloroplasts) subunit where the sequence alignments show five completely or highly conserved residues all positioned in the N-terminal β -sandwich domain (residues from 1 to 84 in the *E. coli* sequence) (Fig. 7 and Fig. 8(B)), three completely or highly conserved residues (G43, G46, and H51 in the bovine sequence) are localized at the interface with subunit *c* facing the interhelical loop of this subunit



В.

A.



 α_{DP}

β_{DP}

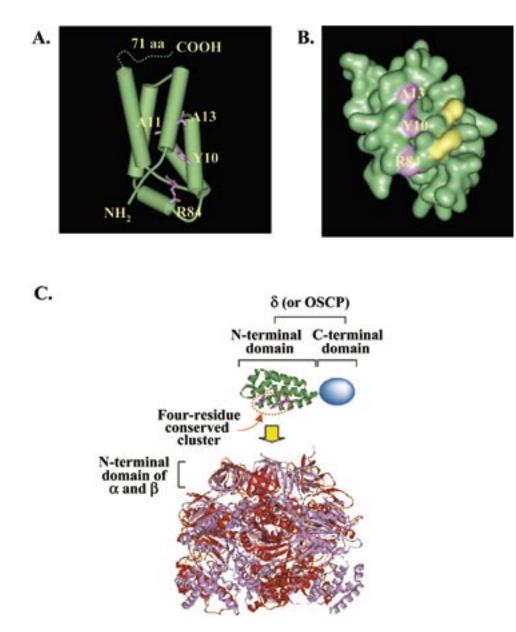


Fig. 4. Location of the highly conserved four-residue cluster in the structure of the N-terminal domain of the bacterial δ subunit, shown in cylinder (A) and surface (B) representations. The residues that form a four-residue conserved cluster in the N-terminal domain, drawn in purple, are located on one side of the molecule, and three of the residues are arrayed in a line on the surface of the molecule. Weakly conserved residues, colored in yellow, are also localized on one side of the molecule around the four-residue conserved cluster. (C) Potential orientation of the conserved cluster of the N-terminal domain of the bacterial δ subunit or mitochondrial OSCP with respect to the $\alpha\beta$ trimer.

(Fig. 8(B) and (C)). On the other hand, the sequence alignment of the γ subunits, and a search for the conserved residues in the structure, show no completely or highly conserved residues at the interface of γ and *c* subunits. Therefore, taken together, we suggest that interactions between subunit *c* and the δ subunit are directly involved in

the reconstitution process of F_1 and F_0 , and that the conserved residues at the interface of the two subunits [Arg41, Gln42 or Asn, and Pro43 in subunit *c* (*E. coli* sequence) and G43, G46, and H51 in mitochondrial δ or the bacterial ε subunit (bovine sequence)], play a key role in rotor connections.

^M Yeast	MFNRVFTRSF
MS. pombe	MNHIFRRSIPITARLPS
MK. lactis	MFSRVFVR
MFriut fly	MASINKLALL
MRat	MAAPATSVLSRQVRS
MBovine	MAALAVSGLSQQVRC
Muman	MAAPAVSGLSRQVRC
MA. thaliana	MANRFRSGISFFKTIAVTDSVSSVRSKSLFPA
^M Sweet potato	MAMTGRARSMGFSILQKALSSAQRSNAHRSILCPTLSNSEL

Bacterial and Chloroplast δ

^C P. purpurea	M
CG. theta	M
^C O. neapolitana	M
CAntithamnion sp.	M
CO. sinensis	M
^C C. caldarium	M
CTobacco	MMAALQQTFITFQSRSPPFTQIISGFTAKLSFSGGLKLPKLT
CPea	MMASLQHTTASLHSKHIPKTTNILTRKPILNLSSSTFYSPKLKLK
Spinach	MAALQNPVALQSRTTTAVAALSTSSTTSTPKPFSLSFSSSTATFNPLRLK
Sorghum	MAALRLASFTLRPAAAAAASASSGATPAAPRSASFARAARGLPS
^C C. reinhardtli	MLAAKSIAGPRAFKASAVRAAPKAGRRTVVVMAR
^B Anabaena sp. PCC 7120	M
⁸ Synechocystis sp. PCC 6803	M
Synechococcus sp. PCC 6301	M
M. genitalium	M
M. gallisepticum	M
M. thermoacetica	M
P. modestum*	M
C. acetobutylicum	M
S. bovis	M
Buchnera sp. APS	M
R. prowazekii	M
T. maritima	M
C. jejuni	M
H. pylori	M
S. typhimurium V. cholerae	M
^B V. alginolyticus	M
^B H. influenzae	M
^B P. multocida	M
^B P. aeruginosa	N
^B X. fastidiosa	N
^B T. ferrooxidans	N
A. ferrooxidans	N
⁸ N. meningitidis Z2491	N
R. capsulatus	M
R. blasticus	M
A. tumefaciens	M
Bacillus sp. PS3	M
B. subtilis	M
B. firmus	H
B. pseudofirmus	M
B. halodurans	<u>H</u>
L. acidophilus	M
^B E. coli	M

Fig. 5. Sequence alignment of OSCP (mitochondria) and δ (bacteria and chloroplasts) subunits. Highly and weakly conserved residues are highlighted in bold and shaded in purple and light yellow, respectively. The residues that form a four-residue conserved cluster in the N-terminal domain (residues 1 to 105 in the *E. coli* sequence) are indicated by arrows. **P. modestum* is Na⁺-ion specific.

	1 11	21	31
M Yeast	ASSLRAAASKAAAPPPVRLFGVEGT	TALYO	A-KNSSIDAAFQSL
^M S. pombe	LGIRSLATATASAHPPVQLYGLDGS	SSLYT/	AV-KESKLDNVEKAL
¹⁴ K. lactis	SMAASAKAGVKPPVQLFGLDGT	TALFT	AS-KTTSVEAAASSL
MFriut fly	SRTLSSAAAQATVKPPVQVFGLEGR	TATALYSI	AS-KLSQLDQVEKDL
MRat	FSTSVVRPFSKLVRPPVQVYGIEGR	TALYS	AS-KOKRLDOVEKEL
MBovine	FSTSVVRPFAKLVRPPVQIYGIEGR	TALYS	AS-KONKLEQVEKEL
Muman	FSTSVVRPFAKLVRPPVQVYGIEGR	TALYSI	AS-KONKLEQVEKEL
MA. thaliana	LRTYATASAQTTANVKVPIALVGENGN		
"Sweet potato	LRNYATASASKEQKIKVPLTMYGVSGN	TASALYL.	AV-KSNTLEKVESEL

Bacterial and Chloroplast $\boldsymbol{\delta}$

P. purpurea			ALLDIAN-EKKAIEQISQDM
G. theta	IAMNNKLAQP		
^C O. neapolitana	SVAKIADA	YAP.	LLELAN-SNKSLKETTNDM
Antithamnion sp.	SQSILYKIANP		
O. sinensis	SINPLASKIAAP	TAR.	ALFDFSV-DQNLMHQITADE
C. caldarium	HNNYKIAKV	YAE	GLFEIAN-TENSLAEINEQL
Tobacco	IKLRSNRTSRRGGGAAGSKMVASAAGS	TAN	LADIAK-SNGTLEOTTADL
Pea	LKLPLTKTRRSTGGALGARMSSLAAGS		
Spinach	ILTASKLTAKPRGGALGTRMVDSTASR	YAS.	ALADVAD-VTGTLEATNSDV
Sorghum	LRLAPPRRRGDLVRPRAEAAADS	ras:	ALSEVAV-ENGTLEQTVSDL
C. reinhardtii	KNEVSES	YAK.	LVELAD-EKGKLEAVHADV
Anabaena sp. PCC7120	TSKVANTEVAQP		
Synechocystis sp. PCC 6803	KGSLYSSKIAEP	YA0	LIGLAQ-QQNLTEVFGDNL
Synechococcus sp. PCC 6301	TSTSQLFDP	YAR.	ALMAIAR-EQGLEDRFGEDA
⁸ M. genitalium	INAQA	GT	LFOLSE-EOKOVKKIYEEC
M. gallisepticum	DTNIMG	FAR	LVDLAH-EEDKVHLFYDN1
^B M. thermoacetica	SEQNVARR	TAR	ALFNIAR-EQGTAGEFANGL
P. modestum	IEAQVGRR	TAE	IYEIAE-SNDNVKELYETL
^B C. acetobutylicum	YEFLORR	rat.	LYEVGE-KNOKLEEYINDF
S. bovis	DKKTQALVEQ	TAK	SLVEINI-EKDSLAE-LOSE
Buchnera sp. APS	SVADTIARP	TAC	FEIAI-ENNTIEKW-KNI
R. prowazekii	NKDNLIQN		
T. maritima	RFSAVAGR		
^B C. jejuni	ENIIARR		
"H. pylori	QDLKVISKH	TAK	ALKNHTK-SDLALLEEIVVG
S. typhimurium	SEFITVARP		
V. cholerae	SDLTTIARP	TAK	AFDFAV-EKOOLGHW-SOM
¹ V. alginolyticus	=====SDLTTIARP	TAK	AFDFAL-EKDOLDOW-GOM
"H. influenzae	SELTTIARP	Y AK	AFDEAI-EQSAVERW-TEM
P. multocida	SELTTIARP	TAK	AFDFAI-EQNAVERW-ANM
P. acruginosa	======================================	TAK	AFEYAO-AHOOLADW-SAA
"X. fastidiosa	SQALTLARP		
"T. ferrooxidans	ADLITVARP	TAP	LMGWRKRAARNRPGRMH
A. ferrooxidans	ADLITVARP		
N. meningitidis Z2491	AEFATIARP	YAR.	ALFGLAQ-EKSQIESW-LGG
R. capsulatus	SEPASISAAIAGR	YAT.	IFDLAC-EAKGIDALSADV
R. blasticus	AEAASISQGIAER		
A. tumefaciens	PVAETSQGTSGVAER		
Bacillus sp. PS3	NQEVIAKR	TAS	LFOIAL-EOGOLDRIEEDV
^B . subtilis	SGSAVSKR	YAS	ALFDIAN-ESAOLNOVEEEL
B. firmus	SNQAVANR	RY	LFQLAE-EKSILSOVVOEM
B. pseudofirmus	SNQAVANR	YAY	ALFOLAE-EKSILSOVVOEM
B. halodurans	SNHAVANR	N NY	ALFELAQ-EKGLHESFVSEL
^B L. acidophilus	ALSREEVAAR	GT	LFGYAO-DNKVLDTVYDEM
"E. coli	SEFITVARP		
	1	-	21

Mitochond	rial	OSCP
WITTOUT		0.001

	41	51	61	71	81
^M Yeast	QKVES1	WKKNPKLGHI	LLN <mark>P</mark> ALSLKI	RNSVIDAIVE	THKNLDGYVV <mark>N</mark> LLK
^M S. pombe	NKLSG\	LOORPEFEON	ISS <mark>P</mark> WLTREI	KILVSSLTQ	MTG-NEPLLKNFYN
^M K. lactis	NALKET	VVKDTKLTS]	LEN <mark>P</mark> ALSAEI	RNIVVDTLSK	KIN-LDQSVQ <mark>N</mark> LLK
MFriut fly					KLR-FAPATVNLLG
MRat	LRVGQI	LK-DPKVSLJ	VLN P YIKRSI	I <mark>K</mark> VKSLKDITT	KEK-FSPLTA <mark>N</mark> LMN
MBovine					KEK-FSPLTS <mark>N</mark> LIN
MHuman	LRVAQI	LK-EPKVAAS	VLN P YVKRS:	I <mark>K</mark> VKSLNDITA	KER-FSPLTT <mark>N</mark> LIN
MA. thaliana	SEMIE	MKTAPIFAQI	TKD <mark>P</mark> SVPRG	I <mark>R</mark> LAAIRDACD	QAK-FAEPTKNFLS
^M Sweet potato	YDLVE	SKKSPTFSQI	MRDPSVPVD	RVNAIKEICA	QAK-FGDTTQ <mark>N</mark> FLL

Bacterial and Chloroplast $\boldsymbol{\delta}$

CP. purpurea	KLIKDILLQSGKLKYFLAN P LKTIEAKKQVIAATFGD-Q-ISENTLSFLM
CG. theta	TQIKTILHDSVDLSKTLSNPLLSIKAKKEVIKAIFEP-N-ISKNTLKFLL
^C O. neapolitana	NIVSQFLANSSDLKKFLGNPLITRERKKNVLKDVLGE-Q-ISSVSLNFLM
CAntithamnion sp.	SMILEVISKSADLKLFLSNPLVEDNLKKNVLNQLFKD-K-VSDFIVKFLM
^C O. sinensis	QNLEVFLNKTPDLTEYLSNPLISAKSKEEVLNKTLKS-Q-INKETFKFLI
^C C. caldarium	NSIKSVLKQMPEFYYFLVN <mark>P</mark> LISQQI <mark>K</mark> KNTIKIVFNN-N-LDKITL <mark>N</mark> FLL
^C Tobacco	EKIEKISDD-EAVFNFFVS <mark>P</mark> IVGEEK <mark>K</mark> RELVDEIVSSSS-IQPHVANFLN
CPea	DKIEQLFSD-PKVFDYFSS <mark>P</mark> IVEDST <mark>K</mark> RQLIGEFATTSG-FQPHTH <mark>N</mark> FLN
CSpinach	EKLIRIFSE-EPVYYFFAN <mark>P</mark> VISIDN <mark>K</mark> RSVLDEIITTSG-LQPHTANFIN
Sorghum	EKLQKIFAD-ETVAEFFDNPTVPREEKTALIDEIAKSYE-LQPHVVNFIN
^C C. reinhardtii	DAVAGLMKENAKLSALIMN <mark>P</mark> VVESDK <mark>K</mark> RAVLAKIAKEAG-FQQYTI <mark>N</mark> WLN
^B Anabaena sp. PCC 7120	RTLLNLLTENQQLRNFIDN <mark>P</mark> FIAAEN <mark>K</mark> KALIKQILSE-A-SP-YLR <mark>N</mark> FLL
Synechocystis sp. PCC 6803	RSLLTLLQDSPDLSAVLSS <mark>P</mark> VVKDED <mark>K</mark> KSVLRSVLGD-G-GNGYLL <mark>N</mark> FLM
^B Synechococcus sp. PCC 6301	ALFRSTLAASADLRHLLEN <mark>P</mark> TLFSSQ <mark>K</mark> KAVLNQVFGS-S-VHPLVL <mark>N</mark> FLN
^B M. genitalium	HFFLKLMRNFKDGSLSFLLNSYTLTKPDKIRLVDKLFKNHFCQVFVDFLK
^B M. gallisepticum	KVVFDLVKENQDLMSLMNSQVLSKNQKHEIIDVVFKDHLTQTIVDFLK
^B M. thermoacetica	EEVSRTLAENSDFRRVLYHQLIPVRE <mark>R</mark> QKLIDTIFPDINPLLK <mark>N</mark> FLH
P. modestum	NGVMELYNTDKEFKTLVDH <mark>P</mark> LIKRED <mark>K</mark> KEFAKKIFGELEESSLNIIF
C. acetobutylicum	GEIVHLLKNDENINQVVNH <mark>P</mark> QISTSE <mark>K</mark> KKIFMEIFKGKIDEKLLNFLL
S. bovis	TEALLSVFEETNLADFLSSLVVSRDE <mark>K</mark> VKLVRLLQESSSVYMNNFLE
Buchnera sp. APS	LIFIKTIASHKKFKNFLSGSISP <mark>K</mark> YLSLIFITIGTNIIDENAK <mark>N</mark> LIK
R. prowazekii	TLLNSIIEDSFEIKKFLFS <mark>P</mark> LVNKID <mark>K</mark> INVFNSLVKTTN-FNKIVN <mark>N</mark> FLL
^a T. maritima	RFLDLVCQIYESSRELFDNPILKPEKKISLIKEIMKSFGQEMDEFQERFL
⁸ C. jejuni	LCILNSAFVLPKFKNIIESNEIKKER <mark>K</mark> MEFLDSFFDIKNSSFQ <mark>N</mark> FLR
^B H. pylori	LKNATEAIRQHKLNQVLAHVSLKVKKEVVFEILEKITSIKACSVLKPVME
⁸ S. typhimurium	LAFAAEVTKNEQMAELLSG-ALAPETLAESFIAVCGEQLDENGQNLIR
^B V. cholerae	LAFTAEVAKNEQMHELLTS-SGSANKLAEIFIAVCGEQLDGHGQNLIK
^B V. alginolyticus	LSFAAEVAKNEQMNELLTG-SVSADKMAEIFVAVCGEQVDTHGQNLLK
^B H. influenzae	LGFAAAVAEDETVKAYLSS-SLSAQKLADTVISICGEQLDQYGQNLIR
^B P. multocida	LHFSSELIKDETMQTFLKS-SLSASKLADTVISICGEQLDQYGQNLIR
^B P. aeruginosa	lgvlaavsoddtvrollke <mark>p</mark> oltssa k aoslidvcgdklnapao <mark>n</mark> fvr
^B X. fastidiosa	LTFSAQVANNPIAAALLCHPQIDHEQAAALLSPEGADPAYVRFLE
^B T. ferrooxidans	CRRLPAMIADVQAQAFLTDPERRDAEKVSLLSAVPVAVDVKAWKAFLA
¹¹ A. ferrooxidans	CRRLPAMIADVQAQAFLTDPERRDAEKVSLLSAVPVAVDVKAWKAFLA
^{II} N. meningitidis Z2491	LEKLAAVVQEGKVASLIDR <mark>P</mark> ETNASE <mark>K</mark> ADILIDLVGLKDKE-LK <mark>N</mark> FVI
^B R. capsulatus	DALTAALAGSAELRDLISS <mark>P</mark> VYTREEQGDAIAAVAAKMG-LSAPLA <mark>N</mark> GLK
^B R. blasticus	DALKDVLAGSPDLGAMIAS <mark>P</mark> VISRGDQAKAVAAIAGKNG-LSPLMT <mark>N</mark> TLA
^B A. tumefaciens	DKFGALLDESDDLKRLVAS <mark>P</mark> VFSAEDQFKAISAICEKAG-IAGLAV <mark>N</mark> FLK
Bacillus sp. PS3	RAVRQALAENGEFLSLLSYPKLSLDQKKALIREAFAG-VSTPVQNTLL
^B B. subtilis	IVVKQVFQNEKALNDVLNH <mark>P</mark> KVPAAK <mark>K</mark> KELIQNAFGS-LSQSVL N TIF
^B B. firmus	ELVKEVVNTTPEFLQLLSH P KVTTEKKRAFIENSFKDSLSETSLHTLL
^B B. pseudofirmus	ELVKEVVNTTPEFLQLLSH P KVTTEK K RAFIENSFKDSLSETSLHTLL
^B B. halodurans	ELIKAVFQDTPELMQFLTH <mark>P</mark> KTELTQ <mark>K</mark> RELLEKTFKGKVNDTIF <mark>N</mark> TLV
^B L. acidophilus	MALKKAAIANPKFISVLSDPILSSKDKK-SILTAVEKDFSDEVQGFLN
^B E. coli	LAFAAEVTKNEQMAELLSG-ALAPETLAESFIAVCGEQLDENGQMLIR
	31 41 51 61 71

	91	101	111	121	131
^M Yeast					AEPEDPKSFKRIEK
^M S. pombe	VLLDN	HRLYLLTRIQKC	FSTLMR-AKE	RGEIEVKIT	ATPLDSKILSRLES
MK. lactis	VLAEN	NRLSLLEHVTSC	FSKLTD-AY	GLVQATVT	AQPLDSKLFKRVEK
MFriut fly	LLADN	GRLKKLDTVINA	YKTIMA-AH	RGEVVCEVV	AKPLDASQSKQLEG
MRat	LLAEN	GRLGNTQGVISA	FSTIMS-VHE	RGEVPCTVT	AFPLDEAVLSELKT
^M Bovinc					ASALDETTLTELKT
MHuman					ASPLEEATLSELKT
MA. thaliana	LLAEN	GRIENLDAIVER	PMQLTN-AHR	RG-VKVL V P	VIPLPPAEEKELTE
^M Sweet potato	ILAEN	GALKHIDRIVKF	FKELTM-AHI	RGEVKATYT	VIP PADEEKELKA

Bacterial and Chloroplast δ

^C P. purpurea	VLVDRK ISMLDVIAGKYLELAY-AMESLTIANIS
CG. theta	VLCDRGRSANLSSIIDNTIELAY-KKASIEIAYVTTATAFSSNQQEALVE
^C O. neapolitana	LLVNRG VAFLDKIACKFLELSY-KODAIEIAKVTESVA SACOOKELAG
CAntithamnion sp.	VLVDRR ISMLHLIIDKYFSLVY-KTESTILTEVITAIDLTEEQEIALIN
^C O, sinensis	VLVNRSRINLLEPIIASYLNLVY-NAASVKMIEVSTAYAFTNLOKNTLIK
^c C, caldarium	ILIERRAIIYFYDIVDOFILIWN-KATNTSVVEIAAVIS TEKOOOYLIN
CTobacco	ILVDMKRVELIKEIVKEREKVYN-TLTDTELAVVTEVVKLESOHLAQIAK
CPea	VLIDSKRIDMIIDIIKEFEFVYN-TLTDTELVVVT VVKLESHHLAQIAK
Spinach	ILIDSERINLVKEILNEFEDVFN-KITGTEVAVVT VVKLENDHLAQIAK
Sorghum	VVVDNFLATILPEIVVEPENIFN-SLTGTEVATVT VVOLESODLAQIAQ
C, reinhardtii	LLVEKDELSLVPEICECFEDLYC-OMTDTOVATLREAVK E0E00FLIAK
^B Anabaena sp. PCC 7120	LLVDKRRIFFLPEILOOYLALLR-OLNOTVLAEVTLAVALTEDOOOAVTE
⁸ Synechocystis sp. PCC 6803	LLVDKR IVFLEAICEOYLALLR-OFTNTVLAEVTALK TDAOKDOVKE
⁸ Synechococcus sp. PCC 6301	LLVDRN IAFLDGIADRYOALLR-KLRNVVRADVSSAVPTTEAQVQVITE
ⁿ M. genitalium	VIILKGYFTLVEQAIKYFFDNVE-SOKHIOFIKIITAFELSSKOLNKIIA
ⁿ M. gallisepticum	VVIDNREFFHIKSIIKKFFRMIE-KEEHTIFINVVIAHEINDOCKAELVE
¹⁰ M. thermoacetica	LVLAKGRERALPEMAAQFRRLVD-QAENILPVEVILAITIREDILAGLKE
"P. modestum	YLIEKDELSSIRGIVAEYLKIYY-AKNOILDVEAIFAIEPTKDOKAKLIE
"C. acetobutylicum	LLIEKKRIHDAEGILTOLNKISL-EKHNKVVAEVRIVIPITDNEKTTLAS
"S. bovis	VILONEREAFLKAILEGVOKDFV-IATNOHDIVVT AVALTDECKERILA
Buchnera sp. APS	LLSENON FNILMNIFERFVKLEA-CYKNIIIVOLKEAFS KENLINKIRK
^B R. prowazekii	LLIKNS THILSNIVEVYNKLLY-ESRNIKIVHVISTNE OPKEOEWIOS
"T. maritima	TLVFERROKLLENIRDLFEYEKILSEOKVPANLSIAHSPEDEELSLLEK
^B C. jejuni	LLIENSKLECIPOIVKELEROKA-FKENIFVGIVY KEK SOENLKDLEV
^B H. pylori	VVLKNNRLCMLELITEELSFDSKRTLEATLLVPEKLENNELEAVOO
"S. typhimurium	VMARNGRINALPDVLEOFIHLRA-VSEATAEVDVILAAALSECOLAEISA
^B V. cholerae	VMAENGELLAIPALYERFAVLKO-EHEKKVDVEVILATELSECORSEIGS
^B V. alginolyticus	VMAENGELAALPDVCTEFYTLKK-EHEKEIDVEVIEATELSDEOLANIGS
"H. influenzae	LMAENKELSAIPAVFEEFKHHVE-EHOAIAEVEVTEAOPENATOIEKIAA
"P. multocida	LMAENKELEVLPAIYOAFOHYVE-EHOKVAEVOVISAOPENATOEOKIAS
ⁿ P. aeruginosa	TVAENKELELLPTIAEMYEOLKA-ECEKSVEVEVTEAFTESKEOODKLAK
¹¹ X. fastidiosa	VIAEAHRLDVLLQVAGLYEKLRA-EAEHVIKAKITEAIELAPNELNNIVT
"T. ferrooxidans	LLIHNDRWPATAEIGTLFADAMR-RAEGVVDVIVINTEAIA DAGOKTAVOS
A. ferrooxidans	LLIHNDRWPATAEIGTLFADAMR-RAEGVVDVIVTEAIA DAGOKTAVOS
¹⁰ N. meningitidis Z2491	VLAGOKHLSILPEVYAOYODLTL-SFNHIKSAVIYHAYPUTDKOVGELAO
"R. capsulatus	LMATKRELFALPOLLKGLAAAIA-EAKGEMTADVTLATALSAAQAEKLAA
"R. blasticus	LMSEKRELFALPOVLSALAGLIA-EEKGEVTAEVTAATKE SAAOAKKLAE
^B A. tumefaciens	VVANNERLFAVPGMIRAYRTIAA-AHRGEITAEVTRAHALDEAQETELKA
Bacillus sp. PS3	LLIERHEFGLVPELAGTVSRPRSTTARGIAKAVAYEGAASTDEELRALSD
B. subtilis	LLIDRHRAAIVPELTDEFIKLAN-VAROTEDAIVYEVKPTDAEMLPLSO
B. firmus	LLVENKRIESLVDMIDSE-KEMSYEAQDMAEAVVYEAKPETSEEQAQIAV
B. pseudofirmus	LLVENKRIESLVDMIDSF-KEMSYEAODMAEAVVYEAKPETSEEQAQIAV
^B B. halodurans	VLVERKHIDLIIPVVOKF-KSLSYDAQKIAEAFVYLAKPLSEAEKDQLSV
^B L, acidophilus	LLLEYNSFADLIDIIDCESLLYD-NENKIASGTATEAVKEDDDOLERLSE
BE. coli	VMAENGRINALPDVLEOFIHLRA-VSEATAEVDVIEAAALSEOOLAKISA
	81 4 91 101 111 121

	141	151	161	171	181
^M Yeast	ALSASKLA	/GQGKSLKLEM	WVVKPEIK <mark>G</mark>	LIVEL <mark>G</mark> DK	TV <mark>D</mark> LSISTKIQK
^M S. pombe	RIAKS-KY	GKGK-LLVS	NKVTPSII <mark>C</mark>	LIVEI <mark>G</mark> DN	ILDVSVGSRLNN
MK. lactis	ALAASSLA	/GKGKSLKLEA	NVVKPEIQ <mark>G</mark>	LIVEVSDR	TVDLSIASRINK
MFriut fly	ALKSFI	KGNESLKIT:	SRV <mark>D</mark> PSII <mark>G</mark>	LIVSI <mark>G</mark> DK	YVNM <mark>S</mark> IATKVKL
MRat	VLNSFI	SKGQILNLE	/KT <mark>D</mark> PSIM <mark>G(</mark>	MIVRI <mark>G</mark> EK	YV DMSAKSKIQK
MBovine	VLKSFI	SKGQVLKLE	/KI <mark>D</mark> PSIM <mark>G(</mark>	MIVRI <mark>G</mark> EK	YV DMSAK TKIQK
MHuman	VLKSFI	SQGQVLKLE	AKT <mark>D</mark> PSIL <mark>G</mark>	MIVRI <mark>G</mark> EK	YV DMSV<mark>K</mark>TKIQ K
MA. thaliana	TLQEII	GAGKKITVE	QKI <mark>D</mark> PSIY <mark>G</mark>	LIVEFQQK	VLOMSIRTRAQQ
MSweet potato	TLQEMV	GQGKSVQIE(QKI <mark>D</mark> PTIL <mark>G</mark>	LVVEF <mark>G</mark> QK	VF D M <mark>S</mark> I R TRARQ

Bacterial and Chloroplast δ

^C P. purpurea	KIKAMTSAKEVKLVISVDPEL	ICCFTIQI	GSKVI	TSIRGOLKO
CG. theta	KLKSMTSTEQIKLNITVDKTL	ICCFKVOI	GSKVI	TSIOGOLRO
^C O. neapolitana	KLKLITGAKKIKLALRVEPKL	IGGFTVEI	GSKLI	TSIRGOLKK
CAntithamnion sp.	KIKVMTKGKNVKLITTIDOTL	IGGFIVRI		
^C O. sinensis	KLKELTNAREIRLVITVDSSL	IGGFLIKT	NSKVL	FTIKNOLOK
^C C. caldarium	KLKEITKANYIKLKLKIDPSL	IGGLIIKF	GSNLI	LSLKGKLKN
CTobacco	GVQRLTGSKNVRIKTVIDESL	VACFTIRY	GNSGSKLI	MSVKKQLED
CPea	QVQKLTGAKKVRTKTLLDPSL	VASTVRY	GNTGSKFI	MSVKRKLEE
^C Spinach	GVQKITGAKNVRIKTVIDPSL	VACFTIRY	GNEGSKLV	MSVKKQLEE
CSorghum	HVQKMTGAKNVRLKTQLDPEL	IACFTVQY	GRDGSSLI	MSVRKQIEE
^C C. reinhardtii	KLQELTGSKNIKLKPVIDSSL	IACFVVEY	GSSQI	L <mark>S</mark> V R GQIER
^B Anabaena sp. PCC 7120	KVLALTKARQVELATKVDSDL	I <mark>GG</mark> VIIKV	GSQVI	S <mark>SIR</mark> GQ <mark>L</mark> RR
Synechocystis sp. PCC 6803	RVKQLTGAQAVELETKVDGDI	L <mark>GC</mark> IVIKV	GSQVF	S <mark>SLR</mark> GQ <mark>L</mark> RR
⁸ Synechococcus sp. PCC 6301	KVKQLTGAAGVEIESQVDADL	L <mark>GG</mark> VIIKV	GSQVL	ASL <mark>R</mark> GQ L KR
^a M. genitalium	IMEKRFKTKVVYKTEIDRSL	ISCIRIES	SSHLF	KNV R DE L KR
⁸ M. gallisepticum	KLYKKFASQVKILYQTDPSL	IAGIRIQS	NDLLI	NSIDGKLKL
^B M. thermoacetica	RLAGITRRNIRLSSRVNPEL	I <mark>GG</mark> VVIRL	GDRVL	ASV K KKLEL
^B P. modestum	QLEKKTGKKVNLEVSIDKSI			G <mark>S</mark> V R RQ L DT
^B C. acetobutylicum	KLSAKYNKIIIFKEII <mark>D</mark> KTI		GDDVI	G T I K FK L ES
^B S. bovis	LVAEKFGVKAGKLVENIDESI	L <mark>GG</mark> FVINV	NNKVI	TSIRRQLQE
Buchnera sp. APS	VLERFFLKKTKIIYKVDPNI	LNGMIVKV	NNTIF	LSAQNHLKQ
⁸ R. prowazekii	RIEKELQHKTELFFDIDNTI	I <mark>gg</mark> iviky	DNVLR	Y <mark>S</mark> I K GS <mark>L</mark> EK
^B T. maritima	FVRKYALKDPVFDISIDESL	IAGALVEF	EGFRL	TTVQGR L KR
C laboral	KLNKKFDANIKLNNKISODD	SURTEIPE	LOVELSESN	AVAT CALVEND
^B C. jejuni	VPBVVENMUTVPBBVT9500	OVINDED	DOIDTOLOU	IVAT MALTER
^B H. pylori	KLQARFNAFVEITQDTWS	KK <mark>G</mark> VSLSV	SS-LDLEIG	F <mark>s</mark> kedi <mark>l</mark> kk
^B H. pylori ^B S. typhimurium		KK <mark>G</mark> VSLSV	SS-LDLEIG	GFSKEDILKK GSV <mark>R</mark> GRLER
^B H. pylori ^B S. typhimurium ^B V. cholerae	KLQARFNAFVEITQ <mark>D</mark> TWS AMEKRLS-RKVKLNCKID KLEQRLE-RKVQLNCSVDETL	KK <mark>O</mark> VSLSV MAGVIIRA L <mark>GG</mark> VIIRA	SS-LDLEIG GDMVID GDLVID	GFSKEDILKK GSVRGRLER NSARGRLKR
⁸ H. pylori ⁸ S. typhimurium ⁸ V. cholerae ⁸ V. alginolyticus	KLQARFNAFVEITQDTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVQLNCSVDETL KLEKRLE-RKVKLNCSVDETL	KK <mark>G</mark> VSLSV MAGVIIRA LGGVIIRA LGGVIIRA	SS-LDLEIG GDMVID GDLVID GDLVID	GFSKEDILKK GSVRGRLER NSARGRLKR DSARGRLNR
^B H. pylori ^B S. typhimurium ^B V. cholerae ^B V. alginolyticus ^B H. influenzae	KLQARFNAFVEITQDTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVQLNCSVDETL KLEKRLE-RKVKLNCSVDETL AMEKRLA-RKVKLNCNVDNAL	KK <mark>G</mark> VSLSV MAGVIIRA LGGVIIRA LGGVIIRA IAGVIVRT	SS-LDLEIG GDMVID GDLVID GDLVID EDFVID	GESKEDILKK GSVRGRLER NSARGRLKR DSARGRLNR GSSRGQLTR
⁸ H. pylori ⁸ S. typhimurium ⁸ V. cholerae ⁸ V. alginolyticus ⁸ H. influenzae ⁸ P. multocida	KLQARFNAFVEITQDTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVQLNCSVDETL KLEKRLE-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDAL AMEKRLA-RKVKLNCSLDSSL	KK <mark>S</mark> VSLSV MASVIIRA LGSVIIRA LGSVIIRA LGSVIIRA IASVIVRT IASVIIRT	SS-LDLEIG GDMVID GDLVID GDLVID EDFVID DDFVID	GSVRGRLER NSARGRLER DSARGRLKR GSSRGQLTR GSSRGQLSR
⁸ H. pylori ⁸ S. typhimurium ⁸ V. cholerae ⁸ V. alginolyticus ⁸ H. influenzae ⁸ P. multocida ⁸ P. aeruginosa	KLQARFNAPVEITQDTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVQLNCSVDETL KLEKRLE-RKVKLNCSVDETL AMEKRLA-RKVKLNCNVDNAL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL	KKSVSLSV MASVIIRA LGGVIIRA LGGVIIRA IAGVIIRT IAGVIIRT IGGVIIRA	SS-LDLEIG GDMVID GDLVID GDLVID EDFVID DDFVID GDLVID	GSVRGRLER NBARGRLER DBARGRLNR GSSRGQLTR GSSRGQLSR GSVRGKLAK
 ^bH. pylori ^bS. typhimurium ^bV. cholerae ^bV. alginolyticus ^bH. influenzae ^bP. multocida ^bP. aeruginosa ^bX. fastidiosa 	KLQARFNAPVEITQDTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVQLNCSVDETL KLEKRLE-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDAL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL	KKEVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IAGVIIRT IAGVIIRA IGGVIIRA IGGAVIDT	SS-LDLEIG GDMVID GDLVID EDFVID DDFVID GDLVID GNVVID	FFSKEDILKK GSVRGRLER NSARGRLKR DSARGRLNR GSSRGQLTR GSSRGQLSR GVRGKLAK GSIKSKLTR
 ⁸ H. pylori ⁸ S. typhimurium ⁸ V. cholerae ⁸ V. alginolyticus ⁸ H. influenzae ⁸ P. multocida ⁸ P. aeruginosa ⁸ X. fastidiosa ⁸ T. ferrooxidans 	KLQARFNAPVEITQDTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVQLNCSVDETL KLEKRLE-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDAL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IAGVIVRT IAGVIIRA IGGAVIDT IGGLVIHT	SS-LDLEIG GDKVI GDLVI GDFVI DDFVI GDLVI GNVVI GDLTI	FFKEDILKK GSVRGRLER NSARGRLKR DSARGRLKR GSRGQLTR GSSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ
 ^bH. pylori ^bS. typhimurium ^bV. cholerae ^bV. alginolyticus ^bH. influenzae ^bP. multocida ^bP. aeruginosa ^bX. fastidiosa ^bT. ferrooxidans ^bA. ferrooxidans 	KLQARFNAPVEITQDTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLE-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL	KKOVSLSV MASVIIRA LGSVIIRA LGSVIIRA IASVIVRT IASVIIRT IGSVIIRA IGSAVIDT IGGLVIHT IGGLVIHT	SS-LDLEIG GDMVI GDLVI GDLVI EDFVI DDFVI GDLVI GDLVI GDLTI GDLTI	SFSKEDILKK GSVRGRLER NSARGRLKR DSARGRLNR GSSRGQLTR GSSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ
 ^bH. pylori ^bS. typhimurium ^bV. cholerae ^bV. alginolyticus ^bH. influenzae ^bP. multocida ^bP. aeruginosa ^bX. fastidiosa ^bT. ferrooxidans ^bA. ferrooxidans ^bN. meningitidis Z2491 	KLQARFNAPVEITQDTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIEPEL	KKOVSLSV MASVIIRA LGSVIIRA LGSVIIRA IASVIVRT IASVIIRT IGSVIIRA IGSAVIDT IGGLVIHT IGGLVIHT IGGLVIHT	SS-LDLEIG GDMVID GDLVID CDEVID DDEVID GDLVID GNVVID GDLTIG GDLTIG GDLTIG GDLTIG	SFSKEDILKK GSVRGRLER NSARGRLKR DSARGRLNR GSSRGQLTR GSVRGKLAK GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ LLVQGKLSA
 ^bH. pylori ^bS. typhimurium ^bV. cholerae ^bV. alginolyticus ^bH. influenzae ^bP. multocida ^bP. aeruginosa ⁱⁱX. fastidiosa ⁱⁱT. ferrooxidans ⁱⁱA. ferrooxidans ⁱⁱN. meningitidis Z2491 ⁱⁱR. capsulatus 	KLQARFNAPVEITQDTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSUDSSL AMEKRLS-REVRLHASEDASL ALSARFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIEPEL TLAKQTGKTVKLNVAVDESL	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IASVIVRT IASVIVRT IGGVIIRA IGGAVIDT IGGLVIHT IGGLVIHT IGGLVIHT IGGLVIHT	SS-LDLEIG GDMVID GDLVID EDEVID DDEVID GDLVID GDLVID GDLTID GDLTID GDLTIG GDLTID GSRMID	FFKEDILKK GSVRGRLER NSARGRLKR DSARGRLKR GSRGQLTR GSSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ LSVQGKLSA TTVKAKLAS
 ^bH. pylori ^bS. typhimurium ^bV. cholerae ^bV. alginolyticus ^bH. influenzae ^bP. multocida ^bP. aeruginosa ^bX. fastidiosa ^bT. ferrooxidans ^bA. ferrooxidans ^bN. meningitidis Z2491 ^bR. capsulatus ^bR. blasticus 	KLQARFNAPVEITQOTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIEPEL TLAKQTGKTVKLNVAVDESL TLKAKVGKTVKLNTVDESL	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IASVIVRT IASVIVRT IGGVIIRA IGGVIIRA IGGLVIRA IGGLVIRA IGGLVIRA IGGLIVKL	SS-LDLEIG GDMVID GDLVID CDEVID CDEVID GDLVID GDLVID GDLTID GDLTID GDLTID GSRMID GSRMID GSTMID	FFKEDILKK GSVRGRLER NSARGRLKR DSARGRLKR GSRGQLTR GSSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ LSVQGKLSA TTVKAKLAS TSVKSKLAS
 ^bH. pylori ^bS. typhimurium ^bV. cholerae ^bV. alginolyticus ^bH. influenzae ^bP. multocida ^bP. aeruginosa ^bX. fastidiosa ^bT. ferrooxidans ^bA. ferrooxidans ^bR. capsulatus ^bR. blasticus ^bA. tumefaciens 	KLQARFNAPVEITQOTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSUDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIEPEL TLAKQTGKTVKLNVAVDESL TLKAKVGKTVKLNTVDESL ALKSVTGKDVAISVTVDPSI	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IASVIVRT LASVIVRT LGGVIIRA LGGVIIRA LGGLVIHT LGGLVIHT LGGLVIHT LGGLVKL LGGLIVKL	SS-LDLEIG GDMVID GDLVID CDEVID CDEVID GDLVID GDLVID GDLTID GDLTID GDLTID GSRMID GSRMID GSRQID	FFKEDILKK GSVRGRLER NSARGRLKR DSARGRLKR GSRGQLTR GSSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ LSVQGKLSA TTVKAKLAS TSVKSKLAS TSVKSKLAS
 ^bH. pylori ^bS. typhimurium ^bV. cholerae ^bV. alginolyticus ^bH. influenzae ^bP. multocida ^bP. aeruginosa ^bX. fastidiosa ^bT. ferrooxidans ^bA. ferrooxidans ^bN. meningitidis Z2491 ^bR. capsulatus ^bR. blasticus ^bA. tumefaciens ^bBacillus sp. PS3 	KLQARFNAPVEITQOTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIEPEL TLAKQTGKTVKLNVAVDESL TLKAVTGKDVAISVTVDPSI VFAQKVGKQTLEIENIIDPEL	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IAGVIVRT IGGVIIRA IGGAVIDT IGGLVIHT IGGLVIHT IGGLVKL IGGLIVKL IGGLIVKL IGGLVKRI	SS-LDLEIG GDMVI GDLVI CDEVI CDEVI GDLVI GDLVI GDLVI GDLTI GDLTI GSRMI GSRMI GSRMI GSRQI GSRQI GSRQI GSRQI	SFSKEDILKK GSVRGRLER NSARGRLKR DSARGRLNR GSSRGQLTR GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ LSVQGKLSA TTVKAKLAS TSVKSKLAS TSVKSKLAS TSVKSKLAS
 ^bH. pylori ^bS. typhimurium ^bV. cholerae ^bV. alginolyticus ^bH. influenzae ^bP. multocida ^bP. aeruginosa ^bX. fastidiosa ^bT. ferrooxidans ^bA. ferrooxidans ^bN. meningitidis Z2491 ^bR. capsulatus ^bR. blasticus ^bA. tumefaciens ^bBacillus sp. PS3 ^bB.subtilis 	KLQARFNAPVEITQOTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIEPEL TLAKQTGKTVKLNVAVDESL TLKAKVGKTVKLNTVDESL ALKSVTGKDVAISVTVDPSI VFAQKAGVASLRIRNEVQTDL	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IAGVIVRT IAGVIVRT IGGVIIRA IGGVIRA IGGLVIHT IGGLVIHT IGGLVKL IGGLVKL IGGLVKRI IGGIKVRI	SS-LDLEIG GDMVI GDLVI CDEVI CDEVI GDEVI GDLVI GDLVI GDLTI GDLTI GSRMI GSRMI GSRMI GSRMI GSRMI GSRMI GSRMI GSRMI GNRIY GNRIY	FFKEDILKK GSVRGRLER NSARGRLKR DSARGRLKR GSRGQLTR GSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ LSVQGKLSA TTVKAKLAS TSVKSKLAS TSURTKLST GSVSGQLER GSVSGQLER
 ^bH. pylori ^bS. typhimurium ^bV. cholerae ^bV. alginolyticus ^bH. influenzae ^bP. multocida ^bP. aeruginosa ^bX. fastidiosa ^bT. ferrooxidans ^bA. ferrooxidans ^bN. meningitidis Z2491 ^bR. capsulatus ^bR. blasticus ^bA. tumefaciens ^bBacillus sp. PS3 ^bB. subtilis ^bB. firmus 	KLQARFNAPVEITQOTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIEPEL TLAKQTGKTVKLNVAVDESL TLKAKVGKTVKLNTTVDESL ALKSVTGKDVAISVTVDPSI VFAQKAGVASLRIRNEVQTDL IFAKKVNKAKLLVINVVNKDL	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IASVIVRT IASVIVRT IGGVIIRA IGGLVIRA IGGLVIRA IGGLVIRA IGGLVKL IGGLVKI IGGIKVRI IGGIKVRI IGGIKVRI	SS-LDLEIG GDMVI GDLVI CDEVI DDEVI GDLVI GDLVI GDLVI GDLTI GDLTI GSRMI GS	FFKEDILKK GSVRGRLER NSARGRLKR DEARGRLNR GSRGQLTR GSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ LSVQGKLSA TTVKAKLAS TSVKSKLAS TSURTKLST GSVSGQLER GSVSGQLCR GRVKSQLDR
 ⁸ H. pylori ⁸ S. typhimurium ⁸ V. cholerae ⁸ V. alginolyticus ⁸ H. influenzae ⁸ P. multocida ⁸ P. aeruginosa ⁸ X. fastidiosa ⁸ T. ferrooxidans ⁸ A. ferrooxidans ⁸ R. blasticus ⁸ R. blasticus ⁸ B. acillus sp. PS3 ⁸ B. speudofirmus 	KLQARFNAPVEITQOTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLS-REVRLHASEDASL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIE PEL TLAKQTGKTVKLNVAVDESL TLKAVTGKDVAISVTVDPSI VFAQKVGKQTLEIENIID PEL VFAKKAGVASLRIRNEVQTDL IFAKKVNKAKLLVINVVNKDL	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IASVIVRT IASVIVRT IGGVIIRA IGGAVIDT IGGLVIHT IGGLVIHT IGGLVKL IGGLVKL IGGLVKL IGGLVKL IGGLKKRI LGGLKIRI	SS-LDLEIG GDMVI GDLVI CDEVI CDEVI GDLVI GDLVI GDLVI GDLTI GDLTI GSRMI GS	FFKEDILKK GSVRGRLER NSARGRLKR DSARGRLKR GSRGQLTR GSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ LSVQGKLSA TTVKAKLAS TSVKSKLAS TSURTKLST GSVSGQLER GSVSGQLER GSVSGLQR GSVKSQLDR
 ⁸ H. pylori ⁸ S. typhimurium ⁸ V. cholerae ⁸ V. alginolyticus ⁸ H. influenzae ⁸ P. multocida ⁸ P. aeruginosa ⁸ X. fastidiosa ⁸ T. ferrooxidans ⁸ A. ferrooxidans ⁸ N. meningitidis Z2491 ⁸ R. blasticus ⁸ A. tumefaciens ⁸ B. acillus sp. PS3 ⁸ B. speudofirmus ⁸ B. pseudofirmus ⁸ B. halodurans 	KLQARFNAPVEITQOTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIE FLAKQTGKTVKLNVAVDESL TLKAVTGKDVAISVTVDPSI VFAQKVGKQTLEIENIID PEL VFAKKAGVASLRIRNEVQTDL IFAKKVNKAKLLVINVVNKDL LFAKKVGKAKLLIENIVDPSI	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IAGVIVRT IAGVIVRT IGGVIIRA IGGVIIRA IGGLVIRA IGGLVIRA IGGLVIRA IGGLVKI IGGLVKI IGGLKIRI IGGLKIRI IGGLKIRI	SS-LDLEIG GDMVI GDLVI CDEVI DDEVI GDLVI GDLVI GDLVI GDLTI GDLTI GSRMI GS	FFKEDILKK GSVRGRLER NSARGRLKR DEARGRLNR GSRGQLTR GSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ LSVQGKLSA TTVKAKLAS TSVKSKLAS TSLRTKLST GSVSGQLER GSVSGQLER GSVSGLDR GSVKSQLDR GSIKGQLDV
 ^b H. pylori ^b S. typhimurium ^b V. cholerae ^b V. alginolyticus ^b H. influenzae ^b P. multocida ^b P. aeruginosa ^b X. fastidiosa ^b X. fastidiosa ^b K. fartoxidans ^b A. ferrooxidans ^b N. meningitidis Z2491 ^b R. capsulatus ^b R. blasticus ^b A. tumefaciens ^b B. acitlus sp. PS3 ^b B. speudofirmus ^b B. halodurans ^b L. acidophilus 	KLQARFNAPVEITQOTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSUDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIE PEL TLAKQTGKTVKLNVAVDESL TLKAVTGKDVAISVTVDPSI VFAQKVGKQTLEIENIID PEL VFAKKAGVASLRIRNEVQTDL IFAKKVNKAKLLVINVVNKDL LFAKKVGKAKLLIENIVDPSI SFAKKYDLNAVRLENKVDPSI	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IAGVIVRT IAGVIVRT IGGVIRA IGGVIRA IGGLVIHT IGGLVIHT IGGLVKL IGGLVKL IGGLVKL IGGLVKRI IGGLKIRI IGGLKIRI IGGLKIRI IGGLKIRI	SS-LDLEIG GDMVID GDLVID CDEVID CDEVID GDEVID GDLVID GDLTID GDLTID GDLTID GSRMID GSRMID GSRMID GSRVID GNRIYD GNRIYD GDRIYD GDRIYD GDRIYD GDRIYD GDRIYD GDRIYD	FFKEDILKK GSVRGRLER NSARGRLKR DSARGRLKR GSRGQLTR GSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ LSVQGKLSA TTVKAKLAS TSVKSKLAS TSURTKLST GSVSGQLER GSVSGQLER GSVSGLDR GSVKSQLDR GSVKQLDR GSVKQLDR
 ⁸ H. pylori ⁸ S. typhimurium ⁸ V. cholerae ⁸ V. alginolyticus ⁸ H. influenzae ⁸ P. multocida ⁸ P. aeruginosa ⁸ X. fastidiosa ⁸ T. ferrooxidans ⁸ A. ferrooxidans ⁸ N. meningitidis Z2491 ⁸ R. blasticus ⁸ A. tumefaciens ⁸ B. acillus sp. PS3 ⁸ B. speudofirmus ⁸ B. pseudofirmus ⁸ B. halodurans 	KLQARFNAPVEITQOTWS AMEKRLS-RKVKLNCKIDKSV KLEQRLE-RKVKLNCSVDETL KLEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSVDETL AMEKRLA-RKVKLNCSLDSSL ALSARLS-REVRLHASEDASL ALKKRFD-CEIEVTTGVDHSL ALERRFAGHKVRFREAVDAAL ALERRFAGHKVRFREAVDAAL MLNKRFD-SELKISVEIE FLAKQTGKTVKLNVAVDESL TLKAKVGKTVKLNTTVDESL ALKSVTGKDVAISVTVDPSI VFAQKAGVASLRIRNEVQTDL IFAKKVNKAKLLVINVVNKDL LFAKKVGKAKLLIENIVDPSI	KKOVSLSV MAGVIIRA LGGVIIRA LGGVIIRA IAGVIVRT IAGVIVRT IGGVIRA IGGVIRA IGGLVIHT IGGLVIHT IGGLVKL IGGLVKL IGGLVKL IGGLVKRI IGGLKIRI IGGLKIRI IGGLKIRI IGGLKIRI	SS-LDLEIG GDMVI GDLVI CDEVI CDEVI GDLVI GDLVI GDLVI GDLTI GDLTI GSRMI GS	FFKEDILKK GSVRGRLER NSARGRLKR DSARGRLKR GSRGQLTR GSRGQLSR GSVRGKLAK GSIKSKLTR ASVRGQVQQ ASVRGQVQQ LSVQGKLSA TTVKAKLAS TSVKSKLAS TSURTKLST GSVSGQLER GSVSGQLER GSVSGLDR GSVKSQLDR GSVKQLDR GSVKQLDR

Fig. 5. Continued

MINOCHORDINAL ODGE	
	191
M Yeast	LNKVLEDSI
^M S. pombe	LNKLLSEPI
MK. lactis	LNQVLREAI
MFriut fly	YTDVIQTAA
^M Rat	LSKAMRDLL
^M Bovine	LSRAMREIL
Muman	LGRAMREIV
^M A, thaliana	MERLLREPVDFNNL
MSweet-potato	MERFLREPLNF

Bacterial and Chloroplast δ

^C P. purpurea	MASHLDVAAM
CG. theta	LASHLGSSAI
^C O. neapolitana	ISNLLGA
CAntithamnion sp.	IAFYLETN
CO. sinensis	LAKHLDSVLEI
^c C. caldarium	SPYI=======
CTobacco	IAAOLEIGDIOLAV
CPea	IAAQIDLGDIQLAV
Spinach	IAAOLEMDDVTLAV
Sorghum	ITSEFELPDVPLEV
C. reinhardtii	VADOLTKEMTAKLS
Anabaena sp. PCC 7120	LSLRLSNS
Synechocystis sp. PCC 6803	VGLSLGTAL
Synechococcus sp. PCC 6301	ISISLAA
^B M. genitalium	IMAHFI
M. gallisepticum	LKHQLRTFSKEN
^B M. thermoacetica	LGEHLKRA
P. modestum	IARS
^B C. acetobutylicum	MKKVMLKEE
S. bovis	FKMNLK
Buchnera sp. APS	LSDSLNF
R. prowazekii	IAKCLKNVKIC
^B T. maritima	IAREALKRGEMS
^B C. jejuni	YILKII
^B H. pylori	IEKQVIQSI
^B S. typhimurium	LADVLQS
^B V. cholerae	LSDALQS
^B V. alginolyticus	LSDALQS
^B H. influenzae	LANELQL
^B P. multocida	LANELQL
P. aeruginosa	LAEALKS
X. fastidiosa	LQASLTH
T. ferrooxidans	LARTLRS
A. ferrooxidans	LARTLRS
N. meningitidis Z2491	LYTTMIN
R. capsulatus	LQNAMKEVG
^B R. blasticus	LQNAMKEVG
^B A. tumefaciens	LKLALKEVG
Bacillus sp. PS3	IRRQLIG
^B B. subtilis	IERQLAGENR
B. firmus	LERQLIAGTR
B. pseudofirmus	LERQLIAGTR
B. halodurans	LHRELVSGPRS
L. acidophilus	IRAQIIDEN
E. coli	LADVLQS
	171

	1
Veast	XQL/7L/
K. Ioctis	Maaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa
P. canadensis	MQUVLI
W: saturnus var. mrakii	MQLVLJ
T. rubrum	NI0/
S. pombe	N10
Irish moss	MNVTLQ:
D, discoideum	NENIVEI EQLELASAVVEI
N. crassa	MASTRVLASRLASOMAASAKVARPAVRVAQVSKRTIQTGSPLQTLERTOMTSIVNATTRQAPOKRAYSSEIAQAMVEV
Rat	NYACSKFVSTRSLIPSTSQLLSRPLSAVELKRPQMPTDEGLSCLAVFRPLTSLIPSRS-FQTSAISRDID7/
Bovine	MYTCAKFVSTPSLIRRTSTVLSRSLSAVVVRRPETLTDESHSSLAVVPRPLTTSLTPSRS-FOTSAISRDI07/
Human	MFACAKLACTPSLIBAGSRVAYRPISASVLSRPEASRTGEGSTVFNGACNG-VSQLIGRE-FOTSAISRDI07/
Maize	8
Wheat	N
Tobacco	N
Rapeseeds	N
Soybean	N
Petunia sp.	M
Sunflower	n M
P. thunbergii	MDPLISA
P. purpurea	nDFIISU
O. sinensis	MDSIISA
G. theta	N
Maize	N
Spinach	NPLIAN
Rice	
	NPLIAA
Garden pea	MNPLIAA
C. vulgaris	BELYAN
O. neapolitana	MBPIV3G
Synechococcus PCC6716	MDPLVAS
P. modestum*	MDMVLAKTVVL
H. pylori	NRFLALPFLALVGVAFAHDGGMCGMDNIKS
M. genitalium	NEHVNEILATVGVILQQTQTTQDVMASAKI
M. pneumoniae	NEHVNEILATVGRILHETTTANTNVANESTER
A. acolicus	MMKRIMAIITAIMPAIAMAAEGEASVAKGI
C. acetobatylicum	MNIDSHTFLL/
B. caldotenax	N
B. stearothermophilus	N
Bacillus sp. PS3	N
B. subtilis	N
S. lividans	NBOTLAA
T. ferrooxidans	NDAHTIIVAJ
H. influenzae	NE-TVIT
M. tuberculosis	NDPTIA36
M. leproc	NDPMIAO
B. aphidicola	HESINVD
E. coli	MENLANDI
	1

Fig. 6. Sequence alignment of subunit c. Completely, highly, and weakly conserved residues are highlighted in bold and shaded in red, purple, and yellow, respectively. The TM1 and TM2 below the sequences represent transmembrane helices. The interhelical "loop" region is indicated by a red dotted underline.

	11 21	31	41 51	61 71
"Yeast	AKYIGAGISTIGLI	1 IAIVFAALINGVS	SIKDTVFPMAILGFAL	STATGLECLNVSFLLL GV
¹⁴ K. Incits	AKYIGAGISTIGLI	1 IAIVFSALIQGVS	SLEDTLFPFAILGFAL	STATGIPCLNISFLLL AV
^M P. canadensis	AKYIGAALATIGLL	INTAIVFAALINGTS	SLENTLEPFAILGFAL	STATGLPCLNISFLLL GV
^M W, saturnus var. mrakii	AKYIGAAISTIGTL	INTAIVFAALINGTS	SLENTLFPFAITGFAL	STATGLPCLAVSFTLL GV
"T. rubrum	AKIIGTGLATTGLI	VUI GVVFGALILGVA	SLRGLLFSYALLGFAF	STATGI PALMMAFLLI VA
"S. pambe	ANYIGAGLATIGVI	VUIGLIFSNLISGTS	SVRPHLFSMAILGFAL	TRATGLECLNLAFLII AA
MIrish moss	ASMIGAGLATIGLT	AVGIVESLVMAYA	SLKOOLPGYTILGPAL	TRAVAL PALIMAFLIL T
³⁴ D. discoideum	GEEVGAGLAAIGLT	A VOIVFAAFILAVO	NLRGELPKLAMLGFAL	STAVGLLADMSFLIL S
^M N. crassa	SENLONGSAAIGLT	I GLVFAALLNGVA	ALRGOLFSYALLGFA	VLAIGLFOLNVALNAR T
Rat	ANFIGAGAATVGVA	ANIGTVFGSLIIGYA	NUSLKOOLFSYAILGFAL	STANGLYCLNVATLIL AM
*Bovine	AKFIGAGAATVGVA	ANIGTVFGSLIIGYA	SINGLESYALLOFAL	STANSIFCLNVAFLIL AN
Muman	ARFIGAGAATVGVA	ATTOTVFGSLIIGYA	SLROOLFSYAILGFAL	STANGLECTNVAFLIL AM
Maior	AKSIGAGAATIALA	W IGNVLSSSINSVA	SLAROSFGYAILGFAL	TRAIASPAPHMAFLIS VF
Wheat	AKLIGAGAATIALA	AV IGNVFSSLIRSVA	SLAROLFGYATLGFAL	TRAIALPALMAFLIL VF
³⁴ Tobacco	ARLMGAGAATIALA	AIGHVPSSLIRSVA	SLASOLFGYAILGFAL	TAIALPALMAFLIS VF
^M Rapeseeds	AESIGAGAATIASA	I GNVFSSLIHSVA	SLAROSFGYAILGFAL	THATALPAPHMAPLIL VF
^M Soybean	AKSIGAGAATIASA	VUIGNVFSSLIRSVA	SLANGLFOYAILOFAL	THAIALPALMAFLIL VF
MPetunia sp.	AKSMGAGAATNASA	I GNVLSSSIHSVA	SLAKOLFGYAILGFAL	THANASPAPHMAFLIS VFOVR
MSunflower	ARSICAGANTIASA	AT TONVLSSSINSVA	SLAROSFGYALLGFAL	TATASPAPHMAPLISSVIPIKESKKEG
^c P. thunbergii	SVIAAGLSVGLASI	V COTAAGOAVEGIA	CREAEGEIRGTLLLSLAF	MALTIYGLVVALALL ANPFV
P. purpurea	SVIAAGLAVGLAAI	CGSAAANAVEGIA	C. EVEGRIRGTLLLSIAF	MUSLTINGLVVALSLL ANPYVG
O. sinensis	SVIAAGLAIGLAAI	I OGHAAGQAVEGIA	CTEGENKIRGTLLLSLAF	MALTIYGLVVALALL ANPFNG
G. thesa	SVVASGLSVGLAAT	I COTAAAQAVEGIA	CPEAEGRIRGTLLLSLAP	MELTIYCLVVALALL ANPFTS
Maize	SVIAAGLAVGLASI	V COTAAGOAVEGIA	CTEAEGRIRGTLLLSLAP	MALTINCLVVALALL ANPEVA
Spinach	SVIAAGLAVGLASI	V COTANGOAVEGIA	CPEAECKIROTLLLSLAP	MALTIYCLVVALALL ANPPV
Rice	SVIAAGLAVGLASI	V COTAAGOAVEGIA	CPEAEGEIRGTLLLSLAF	MALTIYCLVVALALL ANPFV
^c Garden pea	SVIAAGLAVGLASI	VI COTANGOAVEGIA	PEAEDKIRGTLLLSLAP	MALTIYCLVVALALL ANPFV
C. vulgaris	SVIAAGLAVGLAAI	COTAAGYAVEGIA	CPEAEGKIRGALLLSPAF	MISLTIYGLVVALALL ANPFAG
CO. neapolitana	SVVAAGLAIGLAAI	I COTAAAQAVEGLA	CTEAEGEIRGTLLLSLAF	NESLTIYOLVVALCLL ANTFAG
Synechococcus PCC6716	SVLAAALAIGLASL	I CONASCOAVEGIA	CUEAEGKIRGTLLLTLAF	MUSLTIYGLVIALVLL ANPFAS
"P. modestum"	ASAVGAGAAMIAGI	V OGYAAGEAVESVA	CUEAKGDIISTMVLGQAI	A STGIYSLVIALILL ANPFVGLLG
"H. pylori	SILGAMIGLGIAAF	MONAAAATITGTA	UNP GVGGKLLTTMFVAMAM	ILAQVITILVFAILAI SNPFLS
^a M. genitalium	GAYIGAGVTMIAGSTV	I COYIFGRAVEAIN	NR EVEROVFELIFICSAV	STAINCLISPILI VACA
[®] M. pneumoniae	GAYIGAGITHVGGATV	L OGYIFGKAVEAVA	NTEVEROVFELIFIGSAI	SESSSITSLIAFILI VSGA
"A. acolicus	LYLGAGLAIGLAGL	W MGHAVRGTORGVA	NINAGGRLQTLMFIGLAF	TIALYCLIAFILL VV
C, acetobutyficum	MQYLGAGLAAIGCI	IGTVTGKAVEAIG	CURSASKVMPTNINGLAF	AUVTSLYALFVAIMLL VK
⁸ B, caldotenax	GVLAAAIAVGLGAL	I NGLIVSRTIEGIA	ELSPVLQTTMFIGVAL	VEALPIIGVVFSFIYLGR
B. stearothermophilus	GVLAAAIAVGLGAL	IANGLIVSRTIEGIN	CHELRPVLQTTMF1GVAL	VEALPIIGVVFSFIYLGR
"Bacillus sp. PS3	GVLAAATAVGLGAL	INGLIVERTIEGIN	CPRLRPVLQTTMFIGVAL	VMALPIIGVVFSFIYLGR
¹⁰ B. saddtilis	NLIAAAIAIGLGAL	I NGLIVSRTVEGIN	EAGKELRTIMFMGIAL	VEALPIIAVVIAFLAF G
S. lividans	EGSLGSIGYGLAAI	VULLIFGNGTOAMA	CPRAAGLIRANQ1LGFAF	CRALALIGLVMPFVYG
T. ferrooxidans	TAIAVGIIPGAAGL	I WGLITSKTIEGIT	CRIMEPOLLVNTFIFAGL	MUSFPEIILAFGFWELMANEFLG
"H. influenzae	TIIGASILLAPAAL	FAILGGEFLESS	CTELASSLOTEMFIVAGL	LOAIANIAVGISLLFI ANPFIGLLN
M. tuberculosis	ALIGOGLIMAGGAI	I DOVAGNALISGVA	C PEAQGRLFTPFFITVGL	VEAAYFINLAFMALEVEATEVE
M. leprac	ALIGGGLIMAGGAI	II DOMAGNALVSGI A	CPEAQSRLFTPFFITVGL	VEAAYFINLAFMALFVEATFVK
B. aphidicola	LYIAVAINIGLAAINA		DLVPLLRTQFFVVMGL	
"E, coli	LYMAAAVMMGLAA1			VAIPMIAVGLGLYVMAVA
	11 21	31 4	1 51	61 71
	TMI	Interi	helical Loop	TM2

Fig. 6. Continued

Length and Dimerization Domain of Mitochondrial Subunit B

The mature mitochondrial subunit *b* is approximately 1.2–1.4 times longer than that of bacterial subunit *b*. Bacterial subunit *b* forms a dimer at its C-terminal domain, and in recent studies using the *E. coli* protein, residues 53–122 were reported to form this dimer, which can span 100–110 Å (Dunn *et al.*, 2000; Revington *et al.*, 1999, 2002). In mitochondrial subunit *b*, no studies have been performed

on the dimerization domain. To predict the dimerization domain of mitochondrial subunit *b*, we aligned and compared sequences of subunits from bacteria, chloroplasts, and mitochondria, and then used the coiled-coil prediction algorithm, which is based on the relative frequency of occurrence of amino acids at each position of the coiled-coil heptad repeat (Lupas *et al.*, 1991).

In the sequence alignment of subunit *b*, no significant homologies are found between mitochondria and bacteria, and between mitochondria and chloroplasts (Data not

ATP Synthases

δ subunit from mitochondria

o subuint from in	1
MY east	MLRSIIGKSASRSLNFVAKRSYAEAAAA
^M A. bisporus	MSSLRLLASARRATTHVAYTR
^M N. crassa	М
^M K. lactis	MFRLSAARTLAKSVNTVVAKR
^M Bovine	MLPSALLRRPGLGRLVRQVRLYAEAAAA
Muman	MLPAALLRRPGLGRLVRHARAYAEAAAA
^M Rat	MLPAALLRHPGLRRLVLQARTYAQAAAS
MC. elegans	MLARTIQRFSVVAKRGYAAAA
"Sweet potato	MFRHSSRLLARATTMGWRRPFSTDLPAETAADSTFVEAWKKLIPNVDPPKTPSAYMAPRP

ε subunit from bacteria and chloroplasts

^c A. columnaris	м
Wheat	м
CBarley	н. М
Maize	M=====================================
Rice	M
^c A. thaliana	M
CSpinach	M
^c Sweet potato	М
Tobacco	М
^c Alfalfa	М
^c Pea	М
Norway spruce	М
^c Japanese black pine	M
^c Liverwort	M
^c C. reinhardtii	M
^c C. vulgaris	M
^c E. gracilis	M
^c C. caldarium	M
^c P. purpurea	M
^c O. sinensis	M
^c P. littoralis	M
Synechocystis PCC6803	M
Anabaena PCC7120	M
Synechococcus PCC6716	M
P. didemni	M
Bacillus sp. PS3	M
B. stearothermophilus	M
B. caldotenax	M
B. megaterium	M
B. subtilis	M
B. firmus	М
E. hirae	М
S. mutans	M
C. acetobutylicum	М
M .thermoacetica	M
M .leprae	M
M.tuberculosis	M
S. lividans	M
V. alginolyticus	M
H. influenzaeRd	1-1 1-1
^a B. aphidicola ^a T. ferrooxidans	n
R. blasticus	M
	M
^a R. capsulatus ^a R. rubrum	M
A. aeolicus	M
A. acoucus H. pylori	M
R. prowazekii	M
E. coli	м
1	M

Fig. 7. Sequence alignment of subunits δ (mitochondria) and ε (bacteria and chloroplasts). Conserved residues are highlighted the same as in Fig. 6

- Ch				
A \$11	hunuf	trom	mitochone	1 *** 9

	11	21	31	41	51
*Yeast	SSGLKLQFAL	PHETL	SGSEVTOVNLPAKS	RICVLAN	VPTVE-QLLPGVVEV
¹⁴ A. bisporus	RGYAEISDKLKLSLAL	PHKAI	SSQDVVQVNIPAES	DMNILSS	VPSIE-PLRPGVVEV
^M N. crassa	-YAEAVADKIKLSLSL	PHOAT	KSQDVVQVNIPAVS	EMIVLAN	VPSIE-QLKPGLVEV
MK. lactis	TYAEAADGALKLQFAL	PHOTL	SGTPVTQVNLPAKS	QINILAN	NVPTVE-QLVPGVVEV
*Bovine	QAPAAGPGQMSFTFAS	PTQVF	NSANVRQVDVPTQT	APPILAN	VPTLQ-VLRPGLVVV
^M Human	PAAASGPNQMSFTFAS	PTQVF	NGANVRQVDVPTLT	AFFILAN	VPTLQ-VLRPGLVVV
^M Rat	PAPAAGPGQMSFTFAS	PTQVF	DGANVRQVDVPTLT	AFBILAS	VPTLQ-VLRPGLVMV
^M C. elegans	PAANANPEELRLTFAS	PDTAV	SNAVVKQVDVPTLA	MVSVLAN	VPTIG-VLKPGVVSV
"Sweet potato	ATPSSIPSKLTVNFVL	PYSSEI	LAGKEVOMVIIPATT	QMUVLPG	VATIA-ELKPGVMSV

$\boldsymbol{\epsilon}$ subunit from bacteria and chloroplasts

A. columnaris	KLNLYVLTPKRII	D-CEVKEIILSTNS	OIN	LPN APINT-AVDMGPLRI
Wheat			_	LPNHAPINT-AVDMGPLRI
Barley				LPNKAPINT-AVDMGPLRI
Maize				LPNHAPINT-AVDMGPLRI
Rice	KLNLYVLTPKRII	D-CEVKEIILSTNS	OIN	LPNHAPINT-AVDMGPLRI
A. thaliana				LANHAPIAT-AVDIGILTI
Spinach				LPNHAPTAT-AVDIGILRI
Sweet potato	TLKLCVLTPNRIV	D-SEVKEIILSTNS	OILI	LPNHAPIAT-AVDIGILRI
Tobacco	TLNLSVLTPNRIV	D-SEVEEIVLSTNS	OIDI	LPNHAPIAT-AVDIGILRI
CAlfalfa	TLNLCVLTPNRTV	D-SEVKEIILSTNS	OIN	LKNHAPIAT-ALDIGILKI
^c Pea				LONHAPIAT-ALDIGILRI
Norway spruce	TLNLRVI.SPNRVI	D-SEVKEIILSTNS	QIV	LPNHASLVA-AVDICVMKI
CJapanese black pine				LPNNASLVA-AVDICVMKI
Liverwort	LNLRIMAPNRIV	N-SDIQEIILSTNS	QIUI	LPNHASVLT-ALDIGIVKI
C. reinhardtii	SLQISILTPERPF	N-GQADEIILPTET	EMEV	LKNHAPIIT-GLNVGAMLI
^c C. vulgaris	TLQVCINTPORIF	N-DQADEIILPTNT	OM V	LTNHAPLIT-ALDIGVTLI
^c E. gracilis	TLDVSIIIPERVE	E-KRVEEIILPTLS	QNEV	LKDHIPILT-GLDIGIILV
C. caldarium	GLNIRVIAPORIV	N-AKAEEVILPTST	QLOI	LSGHAPLLT-ALDIGVMRV
^c P. purpurea	TLNIRIIAPORTV	D-AEAQEIILPSST	QLII	LTGHAPLLT-ALDIGVMRV
^c O. sinensis	VMNVRVLTPTRVI	CS-TTADEVILPGLT	LVOI	LDGMAALIT-ALDTGLLRI
^c P. littoralis	SLNIRVIAPDGLI	D-TTAEGVVLPSLT	QLAI	LTGHAPLIT-SLEIGILRI
*Synechocystis PCC6803	TLTVRVI TP DKVV	D-EEVQELILPSTT	QLI	LSNNAPLLT-ALEIGVMRV
Anabaena PCC7120	TLTVRVI SPDKTV	D-AEVDEVILPSTT	QLUI	LSGRAPLST-ALDTGVLRV
Synechococcus PCC6716	VMTVRVIAPDKTV	D-APAEEVILPSTT	QLI	LSNEAPLLT-ALETGVMRV
P. didemni	TLTLRVI TP DKTV	D-DSVEEIVLPSTT	QVIIV	LTGRAPLLT-ALDTGVMRV
Bacillus sp. PS3	KTIHVSVVTPDGPV	E-DDVEMVSVKAKS	ELII	LPGHIPLVA-PLEISAARL
⁸ B. stearothermophilus				LPGHIPLVA-PLEISAARL
^a B. caldotenax				LPGHIRLVA-PLEISAARL
B. megaterium				LHGHIPMVA-PLQIGAVRL
B. subtilis		a the second states and second		LPG IPTVA-PLKIGAVRL
B. firmus		and the second second second second		FREEIPLVA-PVTVGRVRL
E. hirae				LPKHAPIIV-PLTIDEVRV
S. mutans				LANHENLIA-PLEVHEMKI
C. acetobutylicum				LPNHTDLVA-FLTPTETIL
^a M. thermoacetica				LPEHAPLIT-PLQAGVVTC
*M. leprae				LPRHIPMVAQLVDDNMVRI
M. tuberculosis				LPRHIPLVAQLVDDAMVRV
S. lividans				MPGHQPLLG-VLESGPVTI
V. alginolyticus				FHGHTPLLT-AIKPGMVRI
*H. influenzae Rd				LPGHTPLLT-AIKPGIVKF
[*] B. aphidicola				YPGHTQLLS-IIKPGVIYI
T. ferrooxidans				LPRHAPLLT-GLRPGELRI
R. blasticus				MQG HAP TIT-TLRP <mark>G</mark> ILRA
R. capsulatus				MPG HAP VIL-SLRP <mark>G</mark> ILTV
R. rubrum				MPRHAPLLS-TVRPGVIST
A. aeolicus				LENHMYLMT-LLKPGLVYF
H. pylori				LYGHSNMIT-LLQAGVIEI
R. prowazekii				LPHHVPMIV-NLKAGLVQI
E. coli	=====AMTYHLDVVBAEOOM	S-GLVERIOVTGSE	ELEI	YPGHAPLLT-AIKPGMIRI

Fig. 7. Continued

ATP Synthases

δ subunit from mitocho	na	па
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	61	71	81	91	101	111
"Yeast	M-EGSN	ISKKFFIS GUF AT	VQPDSQLCVT	AIEAFPLESF;	QENIKNLLA	EAKKNVS
"A. bisporus	VEDSGS	OK-WFVS GGF AT	VHPNNRLTIN	WVEAAPLEDF:	SIEAIRANLO	EANKVAA
^M N. crassa	IEESGS	INKQYFLS GUF AV	VQPGSKLSIN	AVEGYALEDF:	SAEAVRAQIA	EAQKIVS
"K. lactis	LEGS	ISKKFFVS GGF AT	VQPDSTLAIT	SVEAFPLESF:	SPENVRSLLA	EAQKNVS
Bovine	HAEDGT	TSKYFVSSCSVT	WNADSSVQL	AEEAVTLOML	LGAAKANLE	KAQSELL
"Human		TSKYFVSS <mark>C</mark> SIA				
"Rat	HAEDGT	TTKYFVSS	VNADSSVQL	AEEVVTLDML	LGAARANLE	KAQSELS
"C. elegans	TTNEGT	VORLEVSSOTLS	VNIDGSCOVI	AEEVLKVEEI	DESAARAELD	AAQRASG
"Sweet potato	HE-GND	WSKYFVS GUP AF	IHANSFADII	AVEAVPLORI	ANLVQKGLA	EFTQKLN

$\boldsymbol{\epsilon}$ subunit from bacteria and chloroplasts

A. columnaris	RLLNDQWLTAVLWSG RLLNDOWLTAVLWSG					
Barley	RLLNDQWLTAVLWS					
Rice	RLLNDQWLTAVLWS					
A. thaliana	RLLNDQWLTAVLWS					
	RLANQWLTMALMC					
Spinach		PARIGNNE-ITI				
Sweet potato	RLNDQWVTMALMGG					
Tobacco	RLNDQWLTMALMG					
Alfalfa	RLTNQQWVTMALMG					
Pea	RLKDRWLTMALMO	Contraction of the second				
Norway spruce	RLNGQWSTMALMO					
Japanese black pine	RLNGQWSTMAMM					
Liverwort	RLNDQWSTMALMC				_	
C. reinhardtil	RGGQASGSKDEWNSYAIM					
C. vulgaris	RSNSNWNPVALMO					
E. gracilis	RQKSSSDWTSLVVT					
C. caldarium	RITNTWTSIVLF					
P. purpurea	RVDKEWMPIVLL					
O. sinensis	KLNEKWTPIILCG					
P. littoralis	KTNSKWTPIIVLG	FAVIRDDE-VLV	LISG	/EEVIKE	DYSKA	KSILAK <mark>A</mark> KIDLI
Synechocystis PCC6803	RPGKDWQNIAVMG0	FAEVENNE-VKV	LVNG	ELGTTI	DAESA	RQAYTAAQGALI
Anabaena PCC7120	RTSKSQNWQAIALL	FAEVEEDE-VTI	LVNG	SERGDTI	NLEEA	RTAYSOAQTKL
Synechococcus PCC6716	RQEREWVAIALMGO	FAEVENNE-VTV	LVNAJ	ERGDTI	DLETA	KREFSE A QAAVA
P. didemni	RPGKDWQAIALMGC	FAEVENNE-VKV	LVNG	EVGDSI	DKETA	RTEFOOAEONLJ
Bacillus sp. PS3	KKGGKTQYIAVSC	FLEVRPDN-VTI	LAQA	ERAEDI	DVLRA	KARKS-GRTPL
B. stearothermophilus	KKGGKTQYIAFS	FLEVRPDN-VTI	LAQA	ERAEDI	DVLRA	KARKS-GRTPL
B. caldotenax	KKGGKTQYIAVSC	FLEVRPDK-VTI	LAQA	ERAEDI	DVLRA	KARKS-GRTPLA
B. megaterium	KKASSTELVAVSCO	FLEVRPDK-VTI	LAQAJ	ETAEEI	DVARA	EEAKKRAEMRLI
^a B. subtilis	KKDGQTEMVAVSC	FVEVRPDH-VTI	LAQA	ETAEGI	DKERA	EAARQRAQERLA
B. firmus	KKGNSEEQVAVSCO	FVEVRADQ-VTI	LAEA	ELPSAI	DVDRA	RAAKERAESRLA
E. hirac	KRTDSDTHVDWIAVNGO	IMEVRONV-VSI	VADS	ERERDI	DVSRA	ERAKQRAERQ14
S. mutans	KRIDDDSHVDWVAVNG					
C. acetobutylicum	VEEDGSRKKVFTST	ILNVGESE-VSF	MCDAS	SEWPDEI	DIORA	ETAKERAEKRL
^a M. thermoacetica	RRRERAEERVAVS	FLEAGPDQ-VII	LADT	ERSEEI	DVEWA	RQARERAERRLE
M. leprae	EREGEKDLRVAVDG	FLSVTEER-VSI	LAES	EFDSEI	DENAA	KQDAES
M. tuberculosis	EREGEKDLRIAVDGC	FLSVTEEG-VSI	LAES	EFESEI	DEAAA	KQDSES
S. lividans	RTSDGGTVVAAVHGG	FISFADNK-LSL	LAEV	ELSDEI	VHRA	ERKLEQAKTE
V. alginolyticus	VEQHGHEEIIYVSC	MVEIQPGT-ATV	LADT	IRGEEL	DAAKA	EEAKRRAEEQIC
H. influenzae Rd	TLKDGNEEVIYVSGC	FLEVQPNI-VTV	LADI	IRGSEL	DADRI	HEAKRKAEENIV
B. aphidicola	FHKNKTEECLYIS	ILEVQPSV-VSI	LADV	IRGIDL	DRKRV	VKAKKQAEEYFF
T. ferrooxidans	IHGAETEYLFVNGG	ILEIQPEM-VTV	LADS	ERATDI	DEAKA	LAAKQAAEARMA
R. blasticus	VS-AEGTKAYVVTC	FAEISATG-VSV	LAER	VPLDEM	DAKL	MDQLVADASAAS
R. capsulatus	VS-AAGTAEYAVTG	FAEVSGEK-VTV	LAERO	LTRAEL	TAAV	HAEMLAEAKKVA
R. rubrum	YNGGKVQRRIFVAGC	FAEVTEDR-CTV	LADE	FDLASL	SEEAV	RARLOAADDRLE
A. aeolicus	NGDDK-NGIAVTY	VLDVTPCKVLIL	AEEAY	EVGKLPI	PASKL	KEEFEEAVKKM
H. pylori	ETENQKEHIAINWG	YAEVTNER-VDI	LADG	VFIKKES	SDDRD	D-AISRAKKLLE
R. prowazekii	YIYNIHNYENTYLIS					
E. coli	VKOHGHEEFIYLSG		_			
	61	71	81		91	101

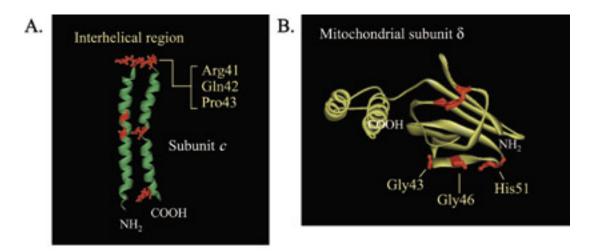
Fig. 7. Continued

δ subunit from mitochondria

lochondria
121 131
SSDAREA-AEAAIQVEVLENLQSVLK
GSGSEADKMEAQIEAEVYEALQHALAK
GGGSQQDIAEAQVELEVLESLQAVLK
SADEVAAAEAAIQLEVLEALQAALK
GAADEATRAEIQIRIEANEALVKALE
GTADEATRAEIQIRIEANEALVKALE
GAADEAARAEIQIRIEANEALVKALEASHVPTLQVL
EGSEVARAEAQIRAEVAEALIKAATNQQ
TASTDVEKAEAQIGVDVHSALNAALTG

ε subunit from bacteria and chloroplasts

KAEGTKDL-VEAKLALRRARIRIEAVNWIPPSN KAEGTKDL-VEAKLALRRARIRIEAVNWIPPSN
KAEGTKDL-VEAKLALRRARIRIEAVNWIPPSN
KAEGTKSL-VEAKLALRRARIRIEAVNWIPPSN
KAEGTKEL-VEAKLALRRARIRVEAVNWIPPSN
RAEGTKEL-VEAKVALRRARIRVEAVNWIPPSN
KAEGKRQT-IEANLALRRARTRVEALNTI
KAEGKRQK-IEANLALRRARTRVEASNTISS
KAEGKRQT-IEANLALRRARTRVEAINAIS
KAEGRRQK-IEANLALRRARTRVEAINPIS
KAEGKRQT-IEANLALRRARTRVETILESINRF
KAEGKRET-IEANLSLRRAKTRVEAIVETIKRIS=-
RAEGKRQA-IEADVALKRARTRLEAISASPPVSN
RAEGKRQA-IEADLALKRARTRLEAINASPPVSN
EAEGNKKKEIEALLVFKRAKARLEAINMASKL
KAEGVKEK-VEANFAYKRAKARYQVVKVLKK
QSQGEKQR-VEATFVFKRARARYQVVKQLGV
MNKDIKRK-FELTLNLKKARARFQVTQLKK
EAKTNKEKFEATOKLRKAKARVOAANTLTNOSIY-
DASSSKEKIEATONIRKARARVOAATAASA
NAETSKARLDASIELKKAVARLEGMNYLS
SAKTTKEIIDASQELKIASAKVKAFKFI
EANRGEDKPNOLKASNNYKKARARLQAAGGAV
QVP-AGDRQAQIQANQAFKRARARFQATGGLA
KAAQSGSKQAQIQAAQAFRRARARLQAAGGVVEI
RANOGDNROELICATOEFKKARARFOAAGGMT
SOODDIDFKRAELALKRAMNRLSVAEMK
SOODIDFKRAELALKRAMNRLSVAEMK
SOODDIDFKRAELALKRAMNRLSVAEMK
SKODDVDVKRAEIALKRAVNRLDISORKF
SOSDDTDIRRAELALORALNRLDVAGK
STKQDAVDFKRAELALKRAINRLDVTGK
EAKEKEDTNELKRATVALHRAINRIKVSKHS
EAKEOHRIDEVORAOVALRRALNRINVGSK
TSNNIDVKRAELSLSRALARIKTKND
ERPPGLDVARAEAALRRAVARLKAAGAI
DDPRIAARGRARLRAVGAID
DDPRIAARGRARLRAVGAID
GDAHAERRADVRLRAAAGR
NOHGDMDFACAASELAKAIAOLRVIELTKKRR
SRG-SDADHDLLVAKLSKELAKLRAYELTEKLLKTRR
KETTNVKKDDVLLEISKAIAKLRVLEIMDKFKK
GHT-DOMEYAAAQAELLEQIARLKTVORLREOGFVR
SVGVDKDTAEKAMSDLOAMKAAAGF
DAAHPSVADAAAKMLADMEALGSHINL
EATSEAEKAEAAQAKAIAEALLAARKG
TAOTMEELKEWEKEAEKARTLLELVEKYR
DASSDRLAVSSVLAKIESL
НОН
SSH-GDVDYAQASAELAKAIAOLRVIELTKKAM



C.

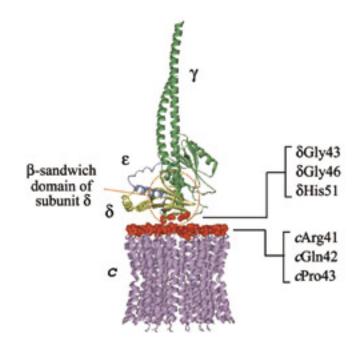


Fig. 8. Conserved interaction sites at the interface of rotors of F_1 and F_0 . The conserved residues in subunit δ (mitochondria) or ε (bacteria and chloroplast) and subunit *c* are numbered according to bovine sequence and *E. coli* sequence, respectively. (A) Location of the conserved residues in the structure of bacterial subunit *c* (1c17; Rastogi and Girvin, 1999). Completely and highly conserved residues are drawn in red. (B) Location of the conserved residues in the structure of mitochondrial δ (1e79; Gibbons *et al.*, 2000). The conserved residues colored in red are located mainly in the N-terminal β -sandwich domain. (C) Interaction of the conserved residues of mitochondrial δ (or ε in bacteria and chloroplasts) with the conserved cluster at the interhelix loop of subunit *c*.

presented). There is some sequence homology between the sequences from bacteria and chloroplasts, but the degree of conservation is fairly low. The sequence alignment of subunit b from nonphotosynthetic eubacteria shows that the homology is fairly weak. Only one residue, Arg36

(*E. coli* sequence), which is located at the region between the membrane spanning helical domain and the coiled-coil dimerization domain, is completely conserved. In contrast, the sequences of mitochondrial subunit *b* are fairly different from those from bacteria and chloroplasts. Apart from

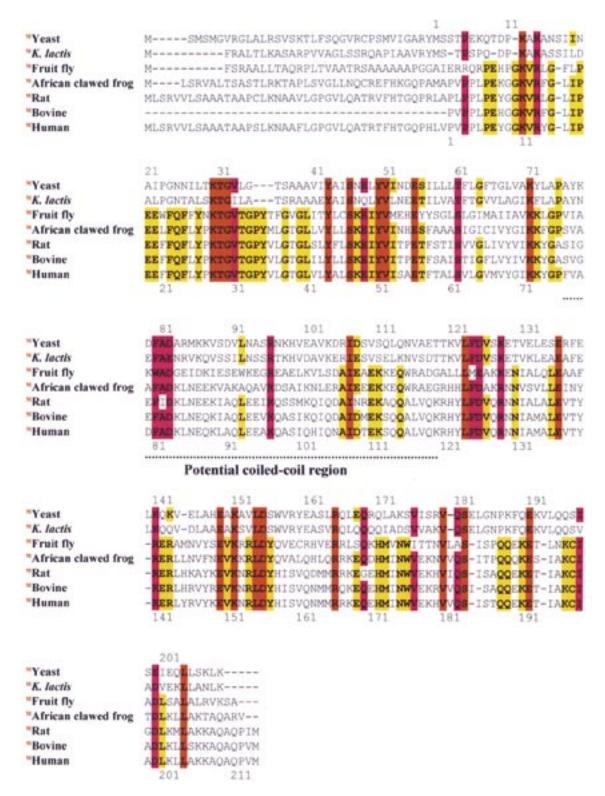


Fig. 9. Sequence alignment of mitochondrial subunit *b*. Conserved residues are highlighted the same as in Fig. 6. The potential coiled-coil region is marked by a dotted line.

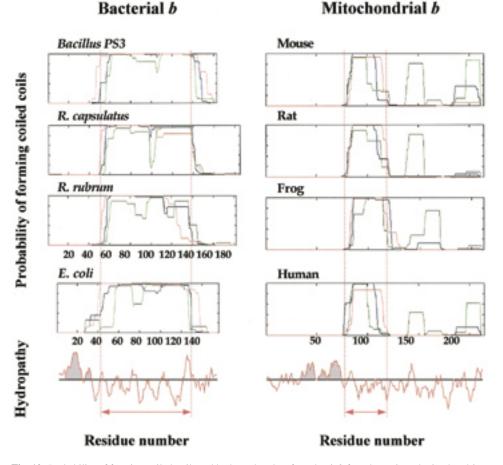


Fig. 10. Probability of forming coiled-coils and hydropathy plots for subunit b from bacteria and mitochondria. The dimerization domain of mitochondrial subunit b is predicted to be about half that of the bacterial b subunit. The predicted membrane-spanning domains are shaded in gray in the hydropathy plots. For the prediction of coiled-coil domain, the algorithm of Lupas *et al.* (1991) was used. It is based on the relative frequency of occurrence of amino acids at each position of the coiled-coil heptad repeat. For the hydropathy plot, the hydropathy index by Kyte and Doolittle (1982) was used.

the length of sequence, the sequence alignment of mitochondrial subunit b from seven different sources shows that more than 20 residues are completely conserved, and that the conserved residues are located fairly even along the sequence (Fig. 9).

In the sequence analysis of bacterial subunit b for the coiled-coil region, as shown in Fig. 10, the sequence from ~ 50 to ~ 130 (or 140) in the *E. coli* sequence is predicted to form a dimer, which is in line with the study on the dimerization domain of the *E. coli* subunit b mentioned above. In contrast, the coiled-coil domain for dimerization in the mitochondrial subunit b is predicted to be much shorter, although the length of the mitochondrial sequences is longer than that of bacterial sequences. Specifically, the dimerization domain of mitochondrial subunit b is predicted to encompass the sequence from about residue 80 to 120 in

the human sequence, which is about half that found for bacterial subunit b. From the sequence alignments and analyses of subunit b, it is interesting to speculate that the mitochondrial subunit b has maintained both high conservation of protein sequences and a shorter dimerization domain for the purpose of interacting with one or more supernumerary subunits.

NOTE

Just prior to the acceptance of this manuscript, a very nice experimental paper was published describing that the helices 1 and 5 in the N-terminal domain of bacterial δ , which is equivalent to mitochondrial OSCP, provide the binding surface of δ to F₁ [Weber, J., Wilke-Mounts, S. and Senior, A. E. (2003). Identification of the F₁-binding

Surface on the δ -subunit of ATP Synthase. *J. Biol. Chem.* **278**, 13409–13416]. The conclusion in the paper obtained using the fluorescence spectroscopic analysis of the Trp residues in the δ subunit well supports our conclusion derived from the bioinformatic analysis of the sequences of mitochondrial OSCP and bacterial/chloroplast δ subunits, that the four-residue conserved cluster in the subunit plays an essential role in the interaction of the subnit with F₁ at the interface.

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